Systemic Lupus Erythematosus

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Faculty

Richelle A. Rennegarbe, PhD, RN, earned her RN degree from Kaskaskia College in Centralia, IL, her BSN from McKendree University in Lebanon, IL and her MS in Community Health Nursing from Southern Illinois University Edwardsville in Edwardsville, IL. She earned her PhD in Health Education from Southern Illinois University Carbondale in Carbondale, IL. Dr. Rennegarbe's primary areas of expertise include community health nursing, women's health issues, nursing management, and chronic conditions including systemic lupus erythematosus. She is a Professor of Nursing, Nursing Division Chair, and Director of the MHA and DNP Programs at McKendree University. Dr. Rennegarbe is certified by the American Organization of Nurse Executives in executive nursing practice.

Faculty Disclosure

Contributing faculty, Richelle A. Rennegarbe, PhD, RN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

Mary Franks, MSN, APRN, FNP-C

Senior Director of Development and Academic Affairs

Sarah Campbell

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The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for nurses working in any healthcare setting who may interact with individuals diagnosed with systemic lupus erythematosus.

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Course Objective

The purpose of this course is to provide nurses with the information necessary to provide appropriate care, guidance, and support for patients who are living with the chronic disease of systemic lupus erythematosus.

Learning Objectives

Upon completion of this course, you should be able to:

1. Identify those individuals at risk for developing systemic lupus erythematosus (lupus).
2. Compare and contrast the four types of lupus.
3. Evaluate the possible causes of lupus.
4. Identify common signs and symptoms of lupus.
5. Select the laboratory tests and diagnostic criteria necessary to appropriately diagnose lupus.
6. Analyze the various treatment options for lupus.
7. Discuss the impact of lupus as a chronic illness.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Systemic lupus erythematosus (SLE), often referred to simply as lupus, is a chronic inflammatory autoimmune disorder of the connective tissue, primarily affecting the skin, joints, blood, and kidneys [1; 2; 3]. In this autoimmune disorder, antibodies are formed within the body that target healthy body systems, causing inflammation and structural changes. The word lupus means "wolf" in Latin, while erythematosus means "redness." The disease is named for the characteristic red rash that appears on the face and is thought to resemble a wolf's face [2; 3]. The term "lupus erythematosus" was coined in 1851 by Pierre Cazenave, a French dermatologist, but writings describing lupus date to ancient Greece [3; 4].

Lupus has been characterized as a multidimensional, unique, complex, challenging, unpredictable, and often elusive disease [2]. It is a non-organ-specific systemic disease with a varying prognosis that can be mild, serious, life-threatening, or even fatal. The disease is characterized by recurring remissions and exacerbations, often called flares, that occur most commonly in the spring and summer [1; 5]. Periods of remission vary considerably among those diagnosed with lupus [2].

EPIDEMIOLOGY

Lupus is more common than other better-known disorders, such as leukemia, multiple sclerosis, cystic fibrosis, and muscular dystrophy, affecting more individuals than all of these diseases combined [3]. The number of reported cases of lupus varies based on different sources; it is believed that there are at least 16,000 patients diagnosed with lupus each year, and more than 1.5 million individuals affected at any given time in the United States. Worldwide, it is estimated that more than 5 million individuals have some form of lupus [6; 8]. However, because lupus is relatively uncommon, difficult to diagnose, and not a reportable disease, epidemiologic studies are often expensive and tend not to produce reliable results on a large scale. Therefore, the CDC notes that recent national estimates of prevalence and incidence are not available for SLE [6]. Further research is required to determine if lupus prevalence and incidence are changing over time [6].

Mortality rates are also difficult collect, but it is currently estimated that 10% to 15% of those diagnosed with lupus will die as a result of the disease [8]. Previously, this percentage was much higher, but improved diagnostic capabilities and treatments have drastically reduced mortality associated with lupus [4]. According to the Centers for Disease Control and Prevention, lupus was identified as the underlying cause of death for an average of 1,176 deaths annually between 2010 and 2016 [6].

Lupus is a significant cause of lost wages and disability in the United States. According to one survey, 55% of patients with lupus reported a complete or partial loss of income due to complications of the disease. One in three have been temporarily disabled by the disease, and one in four were receiving disability benefits [9]. On average, only 46% of people with lupus of working age report being employed [26].

A 2016 study determined that the average annual direct healthcare costs of a person with lupus was approximately $33,000. The average annual productivity cost (i.e., lost hours of economic productivity due to lupus) was between $1,200 and $20,000, making the total average annual cost for patients with lupus as high as $50,000 [7]. In addition, it was found that these estimates may be higher among people with lupus nephritis and more severe or active lupus [7].

More than 90% of SLE cases occur in women, with most women developing symptoms in their childbearing years (15 to 45 years of age) [11]. New diagnoses of SLE in women older than 45 years of age are uncommon [3]. SLE is most common among Black individuals, with Black women having three times the incidence of White American women. The incidence of lupus is also greater in Hispanic, Asian, and Native American women when compared to White women. Statistics show that Black and Hispanic women tend to develop the disease at a younger age, are more likely to develop more serious complications (particularly cardiovascular complications and kidney disease), and tend to have a higher mortality rate from the disease as compared to White women [11].

TYPES OF LUPUS

Four different forms of lupus have been identified: cutaneous lupus erythematosus (CLE), drug-induced lupus, neonatal lupus, and SLE [2]. CLE mainly affects the skin and can be acute or chronic, with skin eruptions that, if left untreated, can lead to scarring and permanent disfigurement. Drug-induced lupus is associated with ingestion of various drugs that result in lupus-like symptoms. Neonatal lupus is a rare, non-systemic condition affecting infants of women with lupus. SLE, which affects multiple organ systems as well as the skin, is considered the most common of the four forms, accounting for 70% of all cases of lupus.

CUTANEOUS LUPUS ERYTHEMATOSUS

CLE is associated with various types of acute and chronic lupus, but the most prevalent form is discoid lupus erythematosus (DLE). DLE is often considered a mild form of lupus, while SLE is the most severe form of the disease [14]. About 20% of individuals with DLE will develop SLE [10].

Symptoms of DLE include lesions that are patchy, crusty, raised, and/or red and scaling, typically non-pruritic plaques, with follicular plugging and central atrophy [2; 5; 10]. The lesions have a "coin-like" or discoid appearance and most commonly appear on the face or scalp, but may appear on any part of the body. Facial lesions may form a "butterfly" pattern. The hair of an individual with DLE tends to be brittle or may fall out in patches. The lesions may resolve completely or result in hypopigmentation, hyperpigmentation, atrophy, permanent hair loss, or permanent scarring [2; 4; 10].

Diagnosis of DLE is based on the patient's history and the rash-like symptoms. A skin biopsy of the lesion reveals immunoglobulins or complement components [2]. SLE must be ruled out in a case of DLE by a negative antinuclear antibody test. Management of DLE includes [2; 12]:

- Avoidance of prolonged sun exposure, fluorescent lighting, or reflected sunlight
- Wearing protective clothing
- Use of sunscreen with a minimum 50 sun protective factor (SPF)
- Avoidance of sun exposure between 10 a.m. and 4 p.m.
- Smoking cessation
- Reporting changes in the lesions
- Initiation of drug therapy that may include the topical, intralesional, or systemic medications used in SLE

Subacute CLE, or SCLE, accounts for 10% of all lupus cases [10; 11]. Nearly half of patients with SCLE also have SLE. This condition is often induced by ultraviolet light exposure, and characteristic lesions present as a red ring-shaped patch with scaly borders and a light center, or scaly red bumps in sun-exposed areas [10; 12]. Unlike DLE, subacute CLE lesions will not usually scar, but there is a potential for skin discoloration, which is often more severe on darker skin.

It is important to note that lupus lesions or rashes may appear different on individuals with brown or black skin. In contrast to the clinically defined "red" or "erythematous" color, lesions or rashes on patients with dark skin may present as dark purple or dark brown, making them easier to overlook. Healthcare professionals should be aware of the varying presentations of cutaneous lupus among individuals with darker skin tones [10].

DRUG-INDUCED LUPUS

Drug-induced lupus occurs as a consequence of the administration of various medications [14]. There are approximately 50,000 new cases of drug-induced lupus reported annually in the United States. Patients with drug-induced lupus tend to be older (between 50 to 70 years of age) than those diagnosed with SLE, mainly due to trends of medication use and polypharmacy in aging populations. No significant statistical difference is apparent in the prevalence for men versus women [15]. Ingestion of specific medications may result in symptoms similar to those seen in SLE, including fever, rash, arthritis pain, and inflammation of the lining around the heart and/or lungs, as well as lab findings consistent with SLE [2]. While more than 30 medications have been linked to the development of drug-induced lupus, three drugs—procainamide, hydralazine, and quinidine—are the cause in 5% to 20% of cases [14; 15]. Other drugs with proven association include carbamazepine, chlorpromazine, isoniazid, methyldopa, minocycline, penicillamine, sulfasalazine and newer tumor necrosis factor (TNF) inhibitors [15]. Drugs with possible association include beta-blockers (such as atenolol and practolol), captopril, cimetidine, lithium carbonate, phenytoin, ethosuximide, methimazole, and statins [2; 3; 15]. The discontinuation of the medication precipitating drug-induced lupus usually results in resolution of the condition [2]. Generally, no other specific treatments are known [15].

NEONATAL LUPUS

Infants born to women with lupus are at risk for a rare condition referred to as neonatal lupus, which is not a true form of lupus. It occurs when an infant passively acquires autoantibodies from a mother with SLE [14]. Approximately 3% of infants born to women with lupus will have this temporary condition [2]. Women with diagnosed lupus should be screened for neonatal lupus during pregnancy by having a maternal blood test between 18 and 24 weeks gestation [2]. Infants with neonatal lupus may experience a rash, blood abnormalities, and liver problems. Most resolve by 6 months of age [14]. Some infants develop potentially serious complete heart block [5; 6; 14]. The heart block is treated with a pacemaker insertion [6]. In addition, approximately 25% of these infants are born prematurely [2].

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

As noted, SLE is a chronic inflammatory autoimmune disorder of the connective tissue and primarily affects the skin, joints, blood, and kidneys [1; 2; 3]. As the most common form of the disease, accounting for nearly 70% of all lupus cases, SLE will be the primary focus of this course [2]. Therefore, the term "lupus" will refer specifically to SLE for the purposes of this course.

ETIOLOGY OF LUPUS

The exact cause of lupus remains a mystery, but many researchers believe that it results from multiple factors [3; 16]. Possible causes may be interrelated and include immunologic dysfunction, genetic factors, hormones, and environmental influences [4; 5].

AUTOIMMUNITY

Immune dysregulation, in the form of autoimmunity, is thought to be the prime cause of lupus. In patients with lupus, the body produces an accelerated inflammatory response, resulting in the production of autoantibodies (antibodies to one's self), causing immune complexes (antigens combined with antibodies) [3; 16]. These autoantibodies and complexes assault the body's own healthy cells and tissues [2; 3; 4; 5]. Antigen-antibody complexes can attack or suppress the body's normal immunity and cause damage to tissues. Symptoms of lupus are the result of the damage to the body's tissues secondary to the immunologic response.

A shortage or functional failure of T lymphocytes is believed to be partially responsible for this autoimmune reaction. Red blood cells, neutrophils, platelets, lymphocytes, or almost any organ or tissue in the body may be attacked. One of the hallmark indicators of lupus is the formation of autoantibodies, and the presence of autoantibodies in the blood is a key factor to the diagnosis of lupus [2; 3; 5].

GENETICS/HEREDITY

The strong hereditary component of lupus is supported by the fact that first- and second-degree relatives of patients with lupus are at a greater risk for developing lupus [17]. Estimates indicate that 5% to 13% of relatives will develop lupus, but only 5% of children whose mothers had lupus will develop the disease [17]. An immediate blood relative with a history of other autoimmune disorders, such as rheumatoid arthritis or scleroderma, also appears to place individuals at greater risk for developing lupus [4].

At this time, researchers have identified several genes linked to an increased susceptibility of lupus and have identified one gene with a direct causative mutation [2; 62]. One study indicated that a human leukocyte antigen (HLA) region that is controlled by genes on the sixth chromosome may be specifically responsible for lupus. The HLA can amplify or perpetuate certain immune and inflammatory responses, particularly autoantibodies [3]. A variant form of the *STAT4* gene has also been associated with an increased risk for developing lupus. Researchers have found that persons with two copies of the disease-risk variant of the *STAT4* gene have more than two times the risk for developing lupus compared to those with no variant form of the gene [18]. In a groundbreaking study published in 2022, researchers were able to pinpoint a single point mutation in the *TLR7* gene of a child with severe lupus and to recreate the development of lupus with specific symptoms in laboratory mice [62]. By confirming that the mutation is a cause of human lupus, new opportunities are afforded to develop treatments [62].

HORMONES

The fact that women in their reproductive years are most susceptible to lupus indicates the possibility of hormone involvement in development of the disease. The female sex hormone estrogen can increase lupus activity [3]. As a result, disease flares may occur with pregnancy, in the days prior to menstruation, or in the postpartum period 2]. The ways in which, and to what degree, sex hormones affect the incidence and severity of lupus remain unclear and are topics of ongoing research.

ENVIRONMENT

For those with a genetic predisposition, environmental factors may trigger lupus [2]. Environmental factors that may precipitate or exacerbate lupus include physical or emotional stress, streptococcal or viral infections, exposure to sunlight, immunizations (live vaccines), surgery, smoking, chemical agents (drugs, metals, or toxins), certain foods or supplements, and other environmental irritants [2; 4; 19]. As noted, the triggering or aggravating of lupus may also occur with pregnancy or an abnormal estrogen metabolism. Research is being conducted to determine the link between stress and the production of stress hormones (adrenaline and cortisone) and the triggering or exacerbation of lupus. Many patients with lupus report initial symptoms or flares with stressful events in their lives, such as divorce, birth, death of a loved one, or loss of a job [2].

SIGNS AND SYMPTOMS ASSOCIATED WITH LUPUS

No two people with lupus will experience identical symptoms. The onset of lupus may be acute or insidious, vague, or even nonspecific. On average, individuals with lupus have symptoms of the disease for two to three years before a diagnosis is made [3]. Symptoms are the result of the inflammatory and immune response of the individual's body to the disease process [3]. Repetitive cycles of exacerbations and remissions of symptoms are a hallmark of the lupus disease process.

GENERAL SYMPTOMS

Common symptoms of lupus include fever, weight loss, malaise, fatigue, skin rashes, polyarthralgia, vasculitis, Raynaud syndrome (discussed in detail later in this course), patchy alopecia (hair loss), and painless ulcers of the mucous membranes [5]. Fatigue is probably the most universal symptom, described as a persistent complaint of a paralyzing fatigue that normal rest may not relieve [2]. Vague symptoms of lupus include aching, fatigue, low-grade or spiking fever, chills, and malaise. Episodic fever is reported by more than 80% of all patients with lupus, with a low-grade fever most often noted [2]. Infection is certainly a major concern and is a potential symptom for patients with lupus. Those with lupus are more susceptible to opportunistic infections due to alterations in their hematologic system, especially in white blood cells. Women with lupus may also experience irregular periods or amenorrhea due to the disease process [2; 3].

DERMATOLOGIC SYMPTOMS

Skin rashes are very common among patients with lupus; approximately 80% of patients report skin involvement [2]. A red, raised rash over the nose and cheeks characterizes the classic malar or "butterfly rash" of lupus. The butterfly rash is reported by 55% to 85% of all patients with lupus at some point during their disease process [2]. Discoid lupus lesions may also be seen. Ultraviolet light often aggravates skin eruptions, and approximately one-third of all patients with lupus are found to be photosensitive [2; 15]. Oral, nasal, and vaginal ulcers may occur. Conditions such as alopecia, pruritus, alteration in wound healing, and bruising are other common dermatologic symptoms.

The British Association of Dermatologists recommends that patients presenting with alopecia areata (i.e., patchy hair loss) undergo serology testing for systemic lupus erythematosus as part of the differential diagnosis.

(https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2012.10955.x. Last accessed October 10, 2023.)

Level of Evidence: Expert Opinion/Consensus Statement

MUSCULOSKELETAL SYMPTOMS

Polyarthralgia (pain in multiple joints) occurs in more than 90% of lupus cases [2]. The joint pain associated with lupus is similar to that experienced by rheumatoid arthritis patients and is often called lupus arthritis. Most patients complain of morning joint stiffness and pain. The pain is typically symmetrical, and joints may become tender, warm to the touch, and swollen. The dominant extremities

are usually more inflamed. Joints commonly affected include the toes, ankles, fingers, wrists, elbows, and knees [20]. Joint pain is often one of the first and most common complaints of those with lupus and is often what initially brings them to a healthcare provider [4]. Additional musculoskeletal symptoms that may occur include subcutaneous nodules, tendonitis, tendon rupture, and carpal tunnel syndrome [2].

HEMATOLOGIC SYMPTOMS

Anemia occurs in approximately 50% of all individuals with lupus [21]. The anemia can result from various factors, including low iron levels, medications, gastrointestinal bleeding, or autoantibody formation to red blood cells [2]. Leukopenia, a decrease in white blood cells, is common in patients with lupus but is rarely significant enough to cause infection [21]. In addition, thrombocytopenia, a low platelet count, may occur [5]. This condition can occasionally result in blood clotting or bleeding problems for patients with lupus [4]. Lymph node enlargement is also a potential symptom of lupus.

GASTROINTESTINAL SYMPTOMS

Two key symptoms in lupus, especially prior to diagnosis, are weight loss and anorexia. These two symptoms are also common to numerous other health conditions and may not be linked to the diagnosis of lupus. Abdominal pain, dysphagia, gastroesophageal reflux, nausea, vomiting, diarrhea, and constipation are also potential symptoms [22]. Hepatic involvement may result in liver enlargement, jaundice, hepatic vasculitis, Budd-Chiari syndrome (blood clot in the portal veins), ascites (fluid accumulation in the abdomen), and abnormal liver function tests [22]. Pancreatitis is another potential complication, occurring in about 5% of patients with lupus [2; 3].

CARDIOPULMONARY SYMPTOMS

Approximately 50% of patients with lupus develop symptoms of cardiopulmonary abnormalities, including pericarditis, myocarditis, myocardial infarction, endocarditis, and tachycardia. Pleurisy, parenchymal infiltrates, dyspnea, pneumonitis, and edema in the extremities are also common. The most common cardiac complication of lupus is pericarditis, while pleurisy is the most common respiratory complication [2; 3].

Vascular symptoms may include vasculitis or Raynaud syndrome. Vasculitis may include necrotic ulcerations that occur most frequently on the lower legs, ankles, and dorsa of the feet [2]. Raynaud syndrome can develop, especially in the digits of the hands and feet, secondary to stress, cold, or vibratory stimuli [3]. This condition is caused by sudden onset of vasospasms of the fingers and toes. The vasospasms cause the digits to tingle and the extremities to turn red, blue, or white in color. In serious cases, it can lead to infarctive lesions, necrotic ulcers, or gangrene. This form of cold sensitivity occurs in approximately 40% of patients with lupus [23].

An additional cardiopulmonary symptom is termed livedo reticularis. This condition occurs due to a disordered blood flow near the surface of the skin [3]. It is a reddish mottling or cyanotic lace-like pattern seen on the arms, legs, or torso of the body, especially apparent in cold weather [2].

RENAL SYMPTOMS

Renal damage is one of the most serious complications of lupus, often causing such symptoms as hematuria, proteinuria, urine sediment, cellular casts, urinary tract infections, and fluid/electrolyte imbalance. Renal involvement has the potential to cause renal failure, affecting up to 50% of patients [2]. Renal disease is a leading cause of death in patients with lupus [2].

CENTRAL NERVOUS SYSTEM SYMPTOMS

Nervous system involvement secondary to lupus is common and can range from mild to severe. Central nervous system involvement may result in cognitive disorders, including confusion, fatigue, memory impairment, and difficulty in articulating thoughts [3]. Cognitive dysfunction is estimated to occur in up to 90% of patients with lupus and is not associated with lupus disease activity [27]. Other neurologic conditions may include convulsive

disorders or seizures, mental dysfunction, stroke, paralysis, behavioral changes or emotional instability, headaches, psychosis, organic brain syndrome, dizziness, irritability, and depression [4; 5]. In addition, those diagnosed with lupus are twice as likely to experience migraine-like headaches [3]. Central nervous system conditions rank only behind renal disease and infection as a leading cause of death for those diagnosed with lupus [2].

OPHTHALMOLOGIC SYMPTOMS

Ophthalmic disease affects approximately 20% of patients with lupus [2]. Ophthalmic symptoms associated with lupus may include a lupus rash on the eyelids, conjunctivitis, dry eyes, glaucoma, and cataracts [2]. In severe cases, retinal exudates or blindness may occur.

DIAGNOSIS OF LUPUS

The diagnosis of lupus may be a challenge for the healthcare provider as well as the patient. A diagnosis of lupus can only be made when an individual shows clinical evidence of multiple organ system disease [24]. It is not uncommon for patients with lupus to have consulted with three to five physicians before a definitive diagnosis of lupus is given [3]. As stated previously, an average delay of two to three years from the onset of symptoms to the time of diagnosis is common [3]. In addition, patients with lupus may have a variety of healthcare professionals caring for them due to multiple organ system involvement and a wide range of symptoms. This may result in confusion and information gaps for the patient and healthcare providers [2].

LABORATORY TESTS

The diagnosis of lupus can be facilitated with a physical examination, extensive patient history, various laboratory tests, and radiographic evaluations [3; 5]. There are several laboratory procedures that help to diagnose and monitor individuals with lupus; these various tests have different implications for the patient (***Table 1***) [2; 3; 5; 24; 25].

The antinuclear antibody (ANA) test is the most specific and sensitive test for lupus and is therefore the most commonly used autoantibody test. Ninety-seven percent of patients with lupus have a positive ANA blood test. The titer and patterns of the blood sample are reported. A titer greater than 1:80 is usually considered positive [24]. It is important to note that a positive ANA test is found in 97% of patients with lupus, but alone, it does not indicate a conclusive diagnosis of lupus [24]. A positive ANA test, although not always found, satisfies one of the four typical clinical characterizations required for a definitive diagnosis of lupus. ANA tests may also be positive in patients with other connective tissue diseases, chronic infectious diseases, and autoimmune diseases [24].

Other laboratory tests are available to assist in diagnosis or to monitor the effects of treatment. The anti-DNA blood test indicates disease activity, especially renal involvement. The anti-DNA test is most often used to monitor response to treatment. In remission, the anti-DNA test response is reduced or absent. In addition, the complement assay levels can assist with the diagnosis and monitoring of active lupus. The most common complements associated with lupus are C_3, C_4, and CH_{50}. When these complement levels are decreased, they can indicate an increase in disease activity [22].

Skin and kidney biopsies can also be used in the diagnosis of lupus. Biopsies assist in determining disease presence in organs as well as tissues. Kidney biopsy determines the disease stage and extent of renal involvement secondary to lupus. A chest x-ray can identify pleurisy or lupus pneumonitis, while an electrocardiogram can be used to indicate conduction defects that may occur with cardiac involvement or pericarditis.

LABORATORY TESTS AND THEIR IMPLICATIONS IN LUPUS	
Laboratory Tests	**Implications**
Complete blood count (CBC) (includes red blood cells, white blood cells, platelets, hemoglobin, and hematocrit)	Anemia, risk for infection, bleeding disorder
Liver screening panels	Hepatitis, jaundice, hepatic abnormalities
Serum creatinine	Elevated levels present in renal impairment
Antinuclear antibody (ANA) test	Identifies presence of autoantibodies; 97% of patients with lupus have a positive ANA
Syphilis serology test or rapid plasma reagin (RPR)	Syphilis test that may be falsely positive in patients with lupus
Urinalysis	Can indicate the presence or extent of renal disease
24-hour urine or glomerular filtration rate	Measures renal function impairment
Erythrocyte sedimentation rate (ESR)	Measures generalized inflammation
C-reactive protein (CRP)	Measures generalized inflammation
Anti-DNA antibody test	Immunoglobulin specific against DNA; highly specific test for lupus and associated with serious organ-threatening disease; 60% to 80% of patients with lupus have a positive anti-DNA
Anti-Sm antibody test	Immunoglobulin test; highly specific for lupus; 20% to 30% of patients with lupus have a positive anti-Sm
Complement components (C_3, C_4, CH_{50})	Proteins that mediate inflammation. Evaluates kidney involvement and disease over time; low complement levels occur during lupus flares
La antibody test or anti-SSB	Immunoglobulin; co-exists with anti-SSA; associated with neonatal lupus; present in 15% of patients with lupus
Ro antibody test or anti-SSA	Immunoglobulin; found with anti-SSB; associated with neonatal lupus and photosensitivity; present in 20% to 30% of patients with lupus
Antiphospholipid antibody (APL)	Autoantibodies that react with phospholipid; includes anticardiolipin; present in 30% to 40% of patients with lupus
Rheumatoid factor (RF)	Commonly positive in rheumatoid arthritis but may be positive in patients with lupus
Source: [2; 3; 5; 24; 25]	*Table 1*

EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY (EULAR)/AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) DIAGNOSTIC CRITERIA

As noted, lupus is a condition that is often difficult to diagnose due to the significant variation of symptoms among individuals. In 2019, the European Alliance of Associations for Rheumatology (formerly the European League Against Rheumatism) (EULAR) and the American College of Rheumatology (ACR) published updated classification criteria for lupus (***Table 2***) [28]. The EULAR/ACR criteria classifies a person as having lupus if they meet entry criterion of an ANA titer of >1:80, followed by additive weighted criteria (seven clinical and three immunologic) in which the patient must meet one clinical criterion and ≥10 points between the clinical criteria and immunologic criteria [28].

CLASSIFICATION CRITERIA FOR THE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS		
Domain	**Criteria**	**Weight**
Entry Criterion		
Positive antinuclear antibody (ANA) titer	ANA titer of >1.80 on Hep-2 cells or an equivalent positive test (ever)	Must be positive to continue to additive criteria
Additive Criteria, Clinical		
Constitutional	Fever	2
Hematologic	Leukopenia Thrombocytopenia Autoimmune hemolysis	3 4 4
Neuropsychiatric	Delirium Psychosis Seizure	2 3 5
Mucocutaneous	Non-scarring alopecia Oral ulcers Subacute cutaneous OR discoid lupus Acute cutaneous lupus	2 2 4 6
Serosal	Pleural or pericardial effusion Acute pericarditis	5 6
Musculoskeletal	Joint involvement	6
Renal	Proteinuria >0.5 g/24h Renal biopsy Class II or V lupus nephritis Renal biopsy Class III or IV lupus nephritis	4 8 10
Additive Criteria, Immunology		
Antiphospholipid antibodies	Anti-cardiolipin antibodies OR Anti-ß2GP1 antibodies OR Lupus anticoagulant	2
Complement proteins	Low C_3 OR low C_4 Low C_3 AND low C_4	3 4
SLE-specific antibodies	Anti-dsDNA antibody OR Anti-Smith antibody	6
Source: [28]		*Table 2*

TREATMENT

Although it is very difficult to determine the exact number of individuals diagnosed with lupus each year, diagnoses of lupus appear to be increasing. This may be linked to several factors, including improved diagnostic tests, a larger number of individuals seeking health care, increased public awareness, and specific diagnostic criteria. Literature on lupus makes it clear that in order to effectively combat this illness, quick and efficient diagnosis and aggressive treatment is essential [4].

There is currently no cure for lupus, and long-term disease management is required. Due to the variability of lupus symptoms, treatment protocols differ for each individual. The range of treatments, however, are increasing in number and becoming more effective; thus, the disease can be controlled reasonably well in most people. According to the U.S. Department of Health and Human Services (USDHHS), "the best way to treat lupus is to listen to the patient, whether she or he was diagnosed today or years ago" [2]. The ultimate goal of treatment is to suppress immune system abnormalities, prevent disease flares, and reduce inflammation and other complications secondary to lupus [5].

Treatment is based on such factors as symptoms and severity, overall general health, activity level, school and/or family schedule, age, family and social situations, other medical conditions, and financial and insurance considerations [4].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the European League Against Rheumatism, treatment in systemic lupus erythematosus should aim at remission or low disease activity and prevention of flares in all organs, maintained with the lowest possible dose of glucocorticoids.

(https://ard.bmj.com/content/78/6/736. Last accessed October 10, 2023.)

Level of Evidence: 2b/B (Cohort study or low quality randomized controlled trial)

NONPHARMACOLOGIC INTERVENTIONS

Individuals diagnosed with lupus are encouraged to prioritize the following [2; 3; 4; 5]:

- Get plenty of physical and emotional rest.
- Maintain a healthy diet.
- Establish an exercise regimen.
- Avoid sunlight.
- Seek prompt treatment of infection.
- Limit stress.
- Set realistic goals and priorities.
- Maintain effective communication with their healthcare providers.
- Develop a support system, including family, friends, healthcare professionals, community organizations, and organized support groups.
- Avoid triggering or aggravating factors.
- Seek regular health care.

Eight to 10 hours of sleep per night along with naps are recommended for patients with lupus. In addition, individuals with lupus should minimize stress to reduce emotional distress, as well as avoid direct prolonged sunlight, especially during the hours between 10 a.m. and 4 p.m. The use of a sunscreen with a sun protective factor (SPF) of 50 or greater that protects against both ultraviolet A and B rays is recommended along with protective clothing such as long sleeves and a hat [2]. Routine exercise is important to reduce fatigue and maintain joint mobility.

PHARMACOLOGIC INTERVENTIONS

Although there is no cure for lupus, there are several types of drugs available to aid in the treatment and management of secondary symptoms. Among these drug classes are nonsteroidal anti-inflammatory drugs (NSAIDs), monoclonal antibodies, corticosteroids, antimalarials, biologics, and immunosuppressives. In cases of severe lupus kidney disease not helped by pharmacologic intervention, dialysis or kidney transplant may be necessary.

Nonsteroidal Anti-Inflammatory Drugs

In cases of mild disease, little or no medication may be needed [30]. Medications used for mild lupus with little or no organ involvement may include NSAIDs that are used to control arthritis pain, inflammation, and fever. NSAIDs function to control and reduce inflammation secondary to the lupus. Examples of generic NSAIDs include ibuprofen, indomethacin, and naproxen. The major side effects of NSAIDs include gastrointestinal upset, ulcers, and a potential decline in renal function.

Other NSAIDs available for the management of lupus symptoms include selective cyclooxygenase-2 (COX-2) inhibitors [30]. These drugs have been very effective in the reduction of inflammation by selectively controlling the chemicals that cause inflammation in the patient with lupus [2]. While some of the COX-2 inhibitors are considered to be safe, they may increase the chance of blood clots in some at-risk patients [2]. Topical treatment for skin lesions may include corticosteroid creams.

Studies involving COX-2 inhibitors, including rofecoxib, celecoxib, and valdecoxib, have indicated an increased risk of heart attack and stroke associated with long-term use. Specifically, rofecoxib in the form of Vioxx was voluntarily withdrawn from the market by the manufacturer in late 2004. Valdecoxib in the form of Bextra was taken off the market in April 2005 at the recommendation of the FDA, which cited a risk of serious skin reactions as a major cause for concern in addition to an increased risk of heart attack and stroke.

In 2005, a panel of the FDA voted to keep COX-2 inhibitors available to the public with the understanding that the benefits outweigh the risks for many people.

The relative risks and benefits of the COX-2 inhibitors are still being studied, and it is recommended that healthcare professionals keep apprised of the current information on this subject and proper use of these medications.

Monoclonal Antibodies

In 2011, the U.S. Food and Drug Administration (FDA) approved a new drug for the treatment of lupus—the first in more than 50 years [31]. The medication, belimumab, is a human monoclonal antibody that inhibits B-lymphocyte stimulator and acts to suppress abnormal B cells. In clinical studies, belimumab was more effective in lessening disease activity than placebo in patients with mild-to-moderate forms of the disease, although more research is necessary to determine if the drug is effective in patients with African American heritage and in patients with severe manifestations. The drug has been approved to treat patients with active, autoantibody-positive lupus who are receiving standard therapy [13; 31]. It is administered via an intravenous infusion, and infusion reactions may occur. This can be prevented in most cases with pretreatment with an antihistamine. Other possible side effects of belimumab use include fever, diarrhea, and nausea [31]. Two observational studies—one conducted in the United States and one conducted in Canada—found that patients with lupus who received eight or more infusions of belimumab plus standard of care for up to 24 months demonstrated improvements in disease severity and laboratory values. The patients also showed a reduced use of oral steroids and a reduced use of healthcare resources as early as six months from the start of belimumab therapy [32; 33]. In 2019, belimumab was approved by the FDA for pediatric patients 5 years of age or older [54]. Additionally, in 2020, belimumab received approval for use in lupus nephritis [57].

In 2021, the FDA issued approval for anifrolumab, a human monoclonal antibody to type 1 interferon subunit 1, for treatment of adults with moderate-to-severe systemic lupus who are receiving standard therapy [13; 57; 58]. Anifrolumab blocks the biologic activity of type 1 interferon receptors that, when elevated, play a role in the pathogenesis of systemic lupus. The agent has been shown to reduce inflammatory and immunological processes in systemic lupus [13; 58]. Anifrolumab is administered by IV infusion and the most common adverse reactions include infection and upper respiratory tract infection [13]. Anifrolumab is not approved for the treatment of lupus nephritis or lupus affecting the central nervous system. Anifrolumab is often used in combination with other drugs, such as hydroxychloroquine and glucocorticoids [13; 57].

Another monoclonal antibody, rituximab, has shown promise in the management of lupus, though not FDA-approved for the treatment of SLE [13; 59; 60]. Many open-label studies have shown improvements in lupus symptoms with the use of rituximab, including in patients with severe and/or refractory disease, but two large randomized, double-blind studies failed to show major clinical response compared with placebo [59; 60]. EULAR recommends considering the off-label use of rituximab in patients with severe renal or extrarenal disease refractory to multiple other agents [61]. Additional research is ongoing.

Corticosteroids

In moderate-to-severe lupus, corticosteroids may be prescribed. Corticosteroids are also known as, or include, glucocorticoids, steroids, cortisone, and prednisone. Prednisone is used for treating lupus conditions impacting major organs. The drug is responsible for rapidly suppressing the immune system, which results in a reduction of inflammation, pain, and fatigue secondary to the autoimmune response [2; 5]. Prednisone doses are tapered off as soon as symptoms are under control. Prednisone is a very powerful drug with numerous potential side effects, including osteoporosis, osteonecrosis, hypertension, hyperglycemia, coronary artery disease, visual changes, excessive hunger with weight gain, bruising, insomnia, acne, hair loss, and alterations in the immune system, such as increased risk of infection or delayed healing. At doses of more than 40 mg/day, it has also been associated with several neuropsychiatric disorders [34]. Therefore, the dosage is reduced as quickly and safely as possible. Prednisone should not be discontinued suddenly, especially if it is taken for four weeks or longer [2]. Instead, prednisone doses should be tapered off slowly to prevent potential complications.

Immunosuppressives

Cytotoxic or immunosuppressive drugs, such as voclosporin, methotrexate, azathioprine, cyclosporine, cyclophosphamide, and mycophenolate, are the most effective drugs used for serious life-threatening lupus or those taking high doses of prednisone [2]. Cytotoxic drugs are administered intravenously or orally. They are primarily used in patients with lupus-related kidney, lung, or brain complications. Mycophenolate mofetil, an immunosuppressive drug, has been suggested for use specifically in patients with lupus nephritis [35; 36]. These drugs are generally used to reduce rejection of transplanted organs and pose considerable risks [4]. Potential side effects of cytotoxic drugs include fatigue, oral ulcers, gastrointestinal complications, liver complications, ovarian or testicular failure, alopecia, and immunosuppression, including bone marrow suppression [2]. In addition, the use of these drugs may increase the risk of developing future malignancies in patients with lupus [2].

Voclosporin is a novel calcineurin-inhibitor immunosuppressant that received FDA approval in 2021 for use in adult patients with lupus nephritis. Voclosporin is given orally, in combination with other drugs, including hydroxychloroquine, corticosteroids, and/or mycophenolate [13; 57]. Safety and efficacy have not been established when used in combination with cyclophosphamide; the use of these drugs concomitantly is not recommended [13]. Side effects include hypertension (potentially severe), diarrhea, infection, anemia, and headache.

Antimalarials

Hydroxychloroquine sulfate may also be used to treat lupus. This drug is an antimalarial but is used to treat lupus because it focuses on containing the immune response. In addition, it may act as an anticoagulant and cholesterol reducer [5]. Possible side effects of antimalarials include rash, nausea, and headache. A serious potential side effect of antimalarial drugs is retinal damage. An eye examination should be completed before treatment begins and annually thereafter [2].

LUPUS AND REPRODUCTIVE HEALTH IN WOMEN

Lupus usually strikes women in their childbearing years (15 to 45 years of age), and the disease process can impact pregnancy. Women with lupus have a higher incidence of spontaneous abortion, premature delivery, and pregnancy-induced hypertension than those without the disease. In addition, pregnant patients with lupus may have an increased risk for a lupus flare during pregnancy and during the immediate postpartum period, but the association between pregnancy and lupus flares remains controversial—at this time, it is unclear whether flares are caused by pregnancy or are related to spontaneous fluctuations in disease activity [37].

Prior to the mid-1980s, women with lupus were advised not to become pregnant due to a potential for disease flare or miscarriage; the miscarriage rate in the 1960s for women with SLE was 43% [2; 37]. Since then, experts have estimated that 17% of lupus pregnancies end in miscarriage, which is comparable to non-lupus pregnancies (15% to 20%) [37; 38; 29]. However, specific populations still have a higher risk of lupus-related miscarriage. In one study the miscarriage rate was estimated at 45% in Hispanic and Black populations, which may be attributed to higher levels of uncontrolled disease activity, high glucocorticoid exposure, and a higher number of comorbid conditions/complications in these groups [37; 39]. For example, lupus nephritis is significantly more common in Black and Hispanic women, and active lupus nephritis is responsible for a fetal loss rate of 75% [37; 40].

Nonetheless, research and improved treatment have made a substantial difference in the outcomes for pregnancy. Available evidence indicates that a woman with lupus can have a safe, successful pregnancy, particularly if disease activity can be minimized. Those considering becoming pregnant should ideally be symptom-free and not taking lupus medications for at least six months prior to conception [5; 37]. Flare rates in pregnancy are also significantly reduced when patients are in remission for six months prior to conception (7% to 33% versus 61% to 67% in women with active disease at conception) [37]. One small study published in 2020 found that the risk of major flare during pregnancy was low (4.1%) when conception happens during stable disease [29]. Women with lupus should be monitored closely by their physician and an obstetrician throughout the course of the pregnancy. It is recommended that female patients with lupus use reliable birth control to prevent harm to the fetus from drugs used to treat lupus and in order to ensure that conception occurs only during periods of sustained remission [41].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The European League Against Rheumatism recommends women with systemic lupus erythematosus be counseled about the use of effective contraceptive measures (e.g., oral contraceptives, subcutaneous implants, intrauterine device), based on their disease activity and thrombotic risk.

(https://ard.bmj.com/content/76/3/476. Last accessed October 10, 2023.)

Level of Evidence: 1/A (Systematic reviews of randomized controlled trials)

According to the USDHHS, one-third to one-half of women with lupus have an anticardiolipin antibody and lupus anticoagulant [2]. These two autoantibodies have been associated with an increased incidence of miscarriage. Women considering pregnancy or who become pregnant should have blood tests to screen for these two antibodies [37]. Women who have a history of miscarriage and have tested positive for these two autoantibodies can be treated with aspirin and heparin during the pregnancy.

There has been controversy as to whether women with lupus should take oral contraceptives and/or receive hormone replacement therapy (HRT) during menopause. Estrogen is believed to increase the risk of lupus flares; however, research regarding the role of sex hormones in disease flares has been mixed.

A study conducted in 2005 indicated that estrogen contained in oral contraceptives and HRT did not increase the risk of flare in women whose disease is stable [2; 42]. However, an observational study found that the use of combined oral contraceptives, particularly recent initiation of use, increased the risk of developing SLE [43]. There were some concerns regarding the applicability of this study information in women of color. Although there is an increased confidence in the benefits of estrogen outweighing the risks, more research is needed in this area and the patient and physician must always weigh the options and closely monitor signs of potential problems. Additionally, the use of an intrauterine device is not recommended for women with lupus due to an increased risk of uterine infection [2].

LUPUS AS A CHRONIC ILLNESS

Numerous illnesses are considered chronic in nature. Various chronic illnesses include diabetes, asthma, congestive heart failure, and rheumatoid arthritis. Lupus is considered to be a chronic illness due to its cyclical nature of exacerbation and remission of symptoms. Chronic illnesses such as lupus can be challenging to the patient due to the physical, psychological, social, and financial impact of the disease.

When most individuals think about chronic illness, they tend to picture illnesses found predominantly in elderly individuals. Chronic illnesses such as lupus, however, are not limited to a specific age group. In fact, lupus usually strikes individuals in the prime of their life.

Chronic illness and disability not only result in the loss of physical aspects of the individual's life but may also impact the psychological, familial, social, and vocational aspects of the affected individual's life [1]. The impact chronic disease will have on an individual is dependent on various factors, including the nature of the condition, the individual's pre-illness or pre-disability personality, current life circumstances, and the amount of family and social support in the individual's environment [1]. All of these disease factors can impact the patient's perception and experience of lupus. Due to the young age at disease onset, most individuals with lupus can expect to face many years managing their chronic condition.

CHRONIC ILLNESS AND MENTAL HEALTH

In addition to physical symptoms, those with lupus may experience psychological and emotional manifestations that may result from the physical symptoms of and treatments for the disease. Because many individuals who receive the diagnosis of lupus are relieved to finally have a name for the condition that afflicts them, the chronic nature of the condition may not be of immediate importance [44]. Initially, the individual may be more focused on treating the symptoms of lupus rather than the realization that there is no cure. Individuals with lupus face the uncertainty of the disease process, including the unpredictability of disease flares and remissions. Thus, living with a chronic disease like lupus can be overwhelming for patients, marked by uncertainty and the potential loss of function secondary to the disease process [1].

Generally, those with lupus are in the young adult development stage of life when an initial diagnosis is made. Lupus may cause alterations in the individual's ability to achieve specific tasks fundamental to this developmental stage. Common tasks or activities for the young adult's developmental goal achievement generally include gaining independence, achievement of vocational goals, establishment of intimate relationships, social responsibility, childbearing, and childrearing [1]. Limitations in any of these developmental activities for this specific age group can result in challenges for the individual diagnosed with lupus.

The psychological impact of lupus can be variable. Lupus may impact family life, work, sexual activity, social activities, finances, and day-to-day living [4]. The diagnosis of lupus may impact one's current lifestyle and result in a need for changes in that lifestyle pattern. It may affect the ability to maintain employment status, alter financial stability, and create a potential for the loss of a role, status, or independence. Being diagnosed with a chronic illness may result in a wide range of reactions, including anxiety, fear, shock, denial, negative self-esteem and body image, and self-blame [4]. Feelings of isolation, grief, stress, guilt, anger, loss of control, decreased confidence, depression, hopelessness or helplessness, irritability, and suicidal ideations are also common in those with a chronic illness such as lupus [1; 2; 3].

CHRONIC ILLNESS AND DISABILITY

Both the perception and importance that an individual and his or her family attribute to a chronic illness can affect the individual's ability to accept the condition and make the adjustments necessary to cope [1]. Illness and disability can impact the relationships of the person diagnosed with the chronic illness. Individuals may fear the loss of a relationship secondary to their chronic illness condition; therefore, they may try to conceal the impact of the condition on their life in order to maintain the relationship [45].

Baker and Wiginton found that study participants "expressed concern that others in their lives did not understand lupus and failed to acknowledge the seriousness of their conditions due to the symptoms not being readily apparent" [44]. Family and friends may deny that the disease is a problem, fail to assist the individual, or fail to understand the disease, particularly if the individual shows no outward signs of the disease. Falvo terms this "invisible disability" [1]. Lupus is one such invisible chronic illness. Additionally, some people may be uncomfortable being in a relationship with an individual with a chronic illness like lupus. They may not know what to say, worry about saying the wrong thing, or fear that the chronic disease is contagious.

CHRONIC ILLNESS AND RELATIONSHIPS

Sexuality and interpersonal issues may also be impacted by a chronic illness. Physical limitations, lack of energy, pain, alterations in self-image, or other reactions may impact the sexuality of an individual with lupus [1]. However, a lack of pleasure from sex and presence of sexual dysfunction is not typical in women with SLE [3]. A large survey found that only 4% of women have significant sexual problems related to the disease [3]. Open communication and knowledge regarding the lupus disease process can prevent uncertainty and issues regarding sexuality.

Some individuals with a chronic condition like lupus do not want to burden or inconvenience those around them; thus, they attempt to manage the disease on their own. Individuals with a chronic illness should make families aware of the necessity for adjustments or alterations in roles and tasks secondary to the lupus disease process. Families should be aware of the fact that lupus requires ongoing care and treatment to effectively control the disease. It has been suggested that, compared to women, men may feel more uncomfortable or intolerant regarding a chronic illness such as lupus. This may be due to the fact that women have historically had the primary caregiver role, particularly regarding care of the ill [45].

Ongoing management of a chronic disease such as lupus is imperative [46]. Baker and Wiginton found in their research that the majority of the participants engaged in self-management for controlling their lupus [44]. Individuals with lupus who understand the impact of having a chronic illness, as well as the skills necessary to control this type of condition, can increase the likelihood of successful disease management.

COPING WITH CHRONIC ILLNESS

According to Phillips, one of the most central aspects of coping with lupus has to do with gaining control of one's life [4]. The use of effective coping strategies can enable an individual to manage his or her emotions. In research completed on coping, psychological adjustment, and health status among women with lupus, it was found that women who engaged in avoidant coping (failing to engage in coping strategies) were more likely to suffer from depression and had greater fatigue and a lower health status [47]. The researcher also indicated that there is a paucity of research on the psychosocial aspects of lupus, especially regarding coping with lupus and its impact on psychological adjustments and health status [47].

Coping strategies are used "to manage, tolerate, or reduce the stress associated with significant life events and to attempt to restore psychological equilibrium after a stressful or traumatic event" [1]. Coping strategies can be adaptive (effective) or maladaptive (noneffective). Individuals have the propensity to engage in coping strategies that have been previously effective. If coping strategies become ineffective, then he or she can alter strategies in an attempt to cope and manage the chronic illness [1]. It is critical to the individual with lupus that he or she engage in effective coping strategies to reduce stress, maintain psychological well-being, and regain control of the situation. Phillips indicated that successful living with lupus can be achieved by taking charge, seeking information, developing a positive relationship with one's physician, and assisting one's family with adjusting to the diagnosis [4].

Tremendous stress may be associated with managing a chronic illness. The loss of control related to the chronic disease can exacerbate the stress level for an individual. Stress also may be elevated by the compromising of roles and changes in the level of functioning [1]. It is vitally important that an individual's personal perception of the stresses associated with the disease, as well as their capacity to cope, be considered, as perceptions of stress and coping abilities will vary. Ineffective coping and high stress levels in individuals with chronic illnesses can result in depression, which is the most common coping problem in patients with lupus [3].

Considerable emotional support may be required by the patient with lupus to cope with the chronic disease. More than 50% of all individuals with lupus experience emotional problems secondary to their illness [4]. Some individuals are overwhelmed with having a disease. They may find professional counseling to be an important means of managing their condition.

A method called cognitive mapping has been used to ascertain how women with lupus represent their illness [48]. In one study, 20 female patients with lupus were interviewed in the convenience sample and asked to generate major concepts for the question, "When you think of living with lupus, what words come to mind?" In addition, participants determined the positive and negative relationship among the identified words or phrases. The concept mapping procedure generated 355 concepts from 20 participants, with 192 unduplicated concepts. Pain was the most commonly identified concept reported by participants. The report concluded, "although diagnosed with the same illness, women presented with different mental representations of the illness" [48].

In another study, Baker and Wiginton surveyed 38 women to assess their perceptions and coping with lupus. They concluded that many women were relieved to have been diagnosed with lupus, as they finally had a label for their symptoms. Study participants also desired "current and accurate information about lupus" [44].

RESOURCES FOR PATIENTS WITH LUPUS

SOCIAL SUPPORT

Social support can have a positive impact on individuals diagnosed with lupus. Stewart defines social support as "interactions with family members, friends, peers, and health professionals that communicate information, esteem, practical aid, or emotional help" [49]. Stewart found that social support may enhance coping and that these interactions helped to moderate the impact of stressors and promote health [49]. Social support can be gained from various sources, including a spouse or partner, other family members, friends, co-workers, neighbors, volunteers, church members, community members, online or in-person self-help mutual aid groups, or healthcare professionals [49].

Seeking and gaining social support can be difficult when one is experiencing a chronic illness such as lupus because tremendous energy is necessary to maintain social networks [45]. Lupus symptoms, as well as treatment side effects, can present a challenge for individuals in maintenance of their pre-illness social relationships and activities. Furthermore, to gain necessary support, individuals with lupus should understand and then communicate to others what they need to assist them in managing their disease.

Keller noted similar findings in her research on social support and psychological distress in women with lupus. She concluded that "younger women with lupus were more psychologically distressed than older women with lupus and that women with shorter duration since diagnosis were more distressed" [50]. Keller also found that the perception of having social support and being satisfied with the social support were more important than the number of social supports [50]. Thus, perception of and satisfaction with social support has been found to reduce psychological distress.

SUPPORT GROUPS

One important potential source of assistance can be support groups. It has been noted that "participating in a support group can provide emotional assistance, boost self-esteem and morale, and help to develop or improve coping skills" [5]. Successful support groups can assist patients to gain insights into how to live with their lupus [51]. Darner found that women with lupus who had been diagnosed for longer periods of time had a healthier psychosocial adjustment [52]. Therefore, those newly diagnosed with lupus may require more support and interventions to aid in psychosocial adjustment. Findings indicate that "support groups, self-help groups, and peer counseling…may facilitate the individual's achievement of a positive adjustment to the newly diagnosed illness" [52]. Self-help groups offer patient education on lupus disease management, and it is recommended that those newly diagnosed with lupus receive support via peer groups. Darner concludes that "involvement in self-help/support groups by the majority of subjects was thought to have influenced positively the psychological and social adjustment of the SLE women" [52].

Support groups provide an avenue for the exchange of feelings and ideas regarding lupus. Phillips, founder of the Center for Coping, stated "self-help or support groups can be incredibly helpful and are some of the best sources of support for people with lupus" [4]. Support groups also restore a sense of autonomy and self-reliance, resulting in a reduction in dependency for the group participants [53]. These groups can provide ideas on how to effectively cope with serious illness and manage problems associated with the condition. Lupus support groups can help members "realize they have the inner strength to cope with existential dilemmas of life as well as the comfort of knowing there are others like themselves" [51]. Gartner states that "in the case of most chronic illnesses, the issue is care not cure, and the mutual-support group can play a powerful role in helping individuals cope with their illness" [53].

Online social support groups may be an important resource for patients with lupus, especially those who live in rural areas or are unable to leave their homes. Patients may be directed to one of many support groups available online, including LupusConnect (https://www.lupus.org/resources/lupusconnect), or MyLupusTeam (https://mylupusteam.com).

PATIENT EDUCATION

LUPUS FOUNDATION OF AMERICA (LFA)

Studies indicate that learning about one's disease process can aid individuals. In addition, it can increase the likelihood of participation in one's care and improve disease outcome [5]. One important voluntary organization that is dedicated to providing such services is the Lupus Foundation of America (LFA). The LFA's mission is to "improve the quality of life for all people affected by lupus through programs of research, education, support and advocacy. [The LFA is] focused on achieving the following disease-specific outcomes: reduce time to diagnosis; ensure people with lupus have an arsenal of safe and effective treatments; and expand direct services and increase access to treatment and care" [55]. The LFA has created the World Lupus Federation, which has more than 200 groups, with the goal of bringing greater attention to end lupus. The LFA provides education services, referrals, health fairs, newsletters, publications, and seminars, and works toward funding research, accelerating delivery and improving cost of medication, and spreading awareness. Support is provided to patients with lupus and their families and friends through the LFA organization [5]. The foundation's website is https://www.lupus.org. To increase national recognition for lupus, May has been designated as Lupus Awareness Month.

LUPUS RESEARCH ALLIANCE

The Lupus Research Alliance is the "world's largest nongovernment funder of lupus research. The organization aims to transform treatment while advancing toward a cure by funding the most innovative lupus research, fostering diverse scientific talent, stimulating collaborations and driving discovery toward better diagnostics, improved treatments, and ultimately a cure for lupus" [56]. The Lupus Research Alliance provides information, research and clinical trials information, and community outreach for those affected by lupus. Information may be accessed at https://www.lupusresearch.org [56].

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES: LUPUS

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a division of the National Institutes of Health, is a leader and coordinator of biomedical research regarding lupus [5]. NIAMS produces free lupus information that may be accessed online at https://www.niams.nih.gov/health-topics/lupus.

CASE STUDY

Patient A is a woman, 20 years of age, living in a small, rural town. In October, she suddenly begins experiencing fatigue, anxiety, and heart palpitations. She has recently given birth to her second child, a daughter. She contacts her physician, who believes the symptoms are related to the stress of having given birth in addition to caring for her toddler son. The physician recommends that Patient A rest and obtain some help caring for her two small children.

Patient A's symptoms worsen and then gradually resolve. Her family encourages her to take her physician's advice and try to reduce the stress in her life. Approximately two years after the initial symptoms, Patient A begins experiencing abdominal pain. Her rural family physician refers her to an internist in a large metropolitan city 50 miles from her home. The internist examines her and preliminarily determines that due to the patient's age and symptoms, her gallbladder is most likely causing the abdominal pain. The internist prescribes a low-fat diet and advises Patient A to adopt healthy lifestyle practices, including increased physical activity.

Five years after the symptoms initially began, Patient A becomes pregnant with her third child. During the sixth month of her pregnancy, the patient begins to experience problems. She has premature contractions, increased fatigue, headaches, and swelling in her legs. Her physician prescribes bed rest due to overexertion. During the last three months of pregnancy, Patient A remains on bed rest and the pregnancy is monitored with bi-weekly visits and ultrasounds. Her family plays a central role in helping her with housekeeping and childcare for her two children. However, she is forced to take a leave of absence from her job due to the premature labor. She delivers a healthy baby girl in September.

Shortly after the birth of her third child, Patient A begins experiencing new and puzzling symptoms. Her ankles and knees begin to swell, and the edema is noted bilaterally. She also starts to complain of joint pain in her ankles, knees, elbows, wrists, and fingers. Patient A has difficulty climbing a flight of steps or dancing. Rest and over-the-counter pain medication relieve her symptoms, but it is difficult for her to find time for much rest due to the responsibilities of caring for a family and working full-time. Her family is very concerned about her health and wonders why the physician is not able to find a cause for her problems.

The winter brings a new intolerance to low temperatures. While Patient A has never liked cold weather, suddenly she is having a problem with her hands and feet becoming painful and discolored when she is exposed to cold. Her extremities became painful, stiff, and altered in color when exposed to cold temperatures. Patient A finally returns to her rural family physician in March. He is perplexed; he is not sure what was causing the young woman's problems. The physician decides to send Patient A to see a rheumatologist in the same metropolitan area as the internist.

The rheumatologist examines the patient and runs several blood tests. Patient A's ANA test is positive at 1:640. Her lupus erythematosus test or LE cell prep is negative (normal: negative test with no LE cells noted.) The rheumatoid arthritis factor is negative (normal: negative with <60 U/mL), and her sedimentation rate is 62 mm/hour (normal: up to 20 mm/hour for women).

The rheumatologist tells Patient A that he cannot be sure of her condition, but that he is considering the possibility that it could be lupus. He emphatically tells her, however, that it is not a positive diagnosis, and he certainly does not want to label her with such a devastating disease unless he is certain. He prescribes an anti-inflammatory medication, naproxen, and tells her to return home and rest. Patient A is frustrated—no one has been able to find an answer to why she feels so sick. She tries to talk to her family and friends, but they do not seem to understand what she is going through. Even the physicians do not seem to hear what she is telling them.

While medication reduces the pain and swelling in her joints, Patient A continues to experience fatigue, abdominal pain, and intolerance to cold weather. She is frustrated and feels as if no one is listening to her complaints. Her spouse, family, and friends do not understand why she feels so bad when she looks as if there is nothing really wrong with her. To Patient A, it seems as if she will never feel healthy again.

In the summer of the following year, Patient A experiences a strange red, raised rash with itching after having been out in the sun. She has always enjoyed the outdoors, and while she has been sunburned in the past, she has never had a rash. In addition, she begins to develop small, raised sores on her legs and arms. The joint pain, swelling, and fatigue continue.

Convinced that there must be something wrong with her, Patient A begins researching information on rheumatologic conditions. Based on her symptoms and the lab test results performed in the past, she begins to suspect that she has lupus. She begins to inquire around the town in which she lives to determine if anyone knows of a good rheumatologist that they like and trust. She finally locates a rheumatologist and makes an appointment as soon as possible.

At the first visit to the new rheumatologist's office, the physician elicits the patient's long medical history and description of her numerous symptoms. He examines her and obtains lab work, including a CBC, ANA, anti-DNA antibody test, and complement series, as well as a skin biopsy of the lesions on her legs. The skin biopsy results indicate small vessel vasculitis. The following lab results are recorded:

- ANA: 1:640 (normal: No ANA detected in a titer with a dilution 1:32)
- Anti-DNA antibody test: Elevated (normal: low or none)
- Complement assay: Decreased C_3 level at 43 mg/dL (normal: 55–120 mg/dL) and decreased C_4 level at 14 mg/dL (normal: 20–50 mg/dL)
- Red blood cell count: 3.8 million/mm^3 (normal: 4.2–5.4 million/mm^3 for women)
- Hemoglobin: 10.5 g/dL (normal: 12–16 g/dL for women)
- Hematocrit: 35% (normal: 37% to 47% for women)
- White blood cell count: 6,000/mm^3 (normal: 5,000–10,000/mm^3 for women)
- Platelets: 138,000/mm^3 (normal: 150,000–400,000/mm^3)

After completing all of the tests, the rheumatologist sits with the patient and her spouse and tells them that although the tests are pending, he is certain that she has systemic lupus erythematosus. She meets the entry criterion of an ANA titer >1:80 of the EULAR/ACR criteria for diagnosis and has the following additive criteria: butterfly rash/facial erythema (acute cutaneous lupus, 6 points), nonerosive arthritis (joint involvement, 6 points), hematologic or blood disorder (autoimmune hemolytic anemia, 4 points), immunologic disorder (abnormal anti-DNA antibody test, 6 points), for a total of 22 points. Patient A has a positive diagnosis with the entry criterion of ANA titer being met, at least one of the clinical domains being met, and a score of greater than 10 points [28].

The physician describes the disease in great detail to Patient A and her husband and answers all of their questions. The physician believes that the patient has had lupus for more than seven years, beginning with her initial symptoms. A one-month course of prednisone with tapered doses is prescribed. Nabumetone, an anti-inflammatory, is added to the regimen prior to the prednisone being weaned off. He reassures Patient A as she leaves his office that he will be available for her and will help her manage the disease.

As Patient A leaves the rheumatologist's office, her feelings are mixed. She is thankful to finally know she is not crazy and to have a diagnosis. She is also angry and bitter that it took seven years and four physicians to finally find a cause for her symptoms. She is relieved that she can finally tell her family and friends why she has felt so sick. She is also very afraid because she is not certain what her future will hold now that she has been diagnosed with the chronic disease lupus.

This case study provides one example of the physical and psychological experiences associated with lupus. The struggles Patient A experiences in an attempt to diagnose her chronic illness are documented, as well as the vagueness of her symptoms. This woman's experience provides a brief glimpse into the challenges of obtaining a diagnosis and of living with lupus.

CONCLUSION

Lupus is a chronic disease that primarily impacts women in their childbearing years. While the exact cause of lupus is unknown, possible causes include genetic or heredity factors, immunologic dysfunction, and environmental factors. Lupus can impact any system of the body with mild to life-threatening symptoms. The diagnosis of lupus can present a challenge to healthcare providers, as symptoms are often vague. Definitive diagnosis is based on the presence the EULAR/ACR criteria. There is no cure for lupus, but various interventions, including medications, can be utilized to prevent, treat, and halt disease progression. Due to the chronic nature of lupus, patients can expect to face many years of dealing with a disease that impacts multiple facets of their life. Effective coping strategies are essential in the management of any chronic illness, including lupus.

GLOSSARY OF TERMS

American College of Rheumatology (ACR): a professional association of more than 8,500 physicians, health professionals, researchers, medical students, and scientists worldwide.

Anemia: a condition resulting from low red blood cell counts.

Antibodies: special protein substances made by the body's white cells for defense against bacteria and other foreign substances.

Anti-DNA: antibodies to DNA, seen in one-half of those with systemic lupus. Implies serious disease.

Antigen: a substance that stimulates antibody formation; in lupus, this can be a foreign substance or a product of the patient's own body.

Anti-inflammatory: an agent that counteracts or suppresses inflammation.

Antinuclear antibodies (ANA): proteins in the blood that react with the nuclei of cells. Seen in 97% of those with lupus, in 5% of healthy individuals, and in most patients with autoimmune diseases.

Antiphospholipid antibody: antibodies to a constituent of cell membranes seen in approximately one-third of those with lupus. In the presence of a co-factor, these antibodies can alter clotting and lead to strokes, blood clots, miscarriages, and low platelet counts. Also detected in the lupus anticoagulant.

Anti-Sm: anti-Smith antibody; found only in lupus.

Anti-SSA antibody: associated with Sjögren syndrome, sun sensitivity, neonatal lupus, and congenital heart block. Also called anti-Ro.

Anti-SSB antibody: almost always seen with anti-SSA/anti-Ro. Also called anti-LA.

Arthralgia: joint pain.

Autoantibody: an antibody to one's own tissue.

Autoimmunity: immune response to one's own tissue.

Butterfly rash: reddish facial eruption over the bridge of the nose and cheeks, resembling a butterfly in flight.

Complement system: a group of proteins that, when activated, are consumed during and promote inflammation.

Corticosteroid: any anti-inflammatory hormone made by the adrenal cortex.

Cortisone: a synthetic corticosteroid.

C-reactive protein (CRP): nonspecific test to detect generalized inflammation.

Creatinine: a blood test that measures kidney function.

Cutaneous lupus erythematosus (CLE): a form of lupus affecting only the skin; discoid lupus erythematosus (DLE) is the most prevalent form of CLE.

Discoid lupus erythematosus (DLE): a form of cutaneous lupus erythematosus affecting only the skin and characterized by a thick, plaque-like rash.

Erythema: having a reddish hue.

Erythrocyte sedimentation rate (ESR): nonspecific test to detect generalized inflammation.

European Alliance of Associations for Rheumatology (EULAR): a professional organization representing people with arthritis/rheumatism, health professionals, and scientific societies of rheumatology in all European nations. Formerly known as the European League Against Rheumatism.

Flare: increased activity of the disease process with an exacerbation of physical manifestations and/or increase in abnormal laboratory test values.

Hematocrit: a measurement of red blood cell levels. Low levels produce anemia.

Hemoglobin: oxygen-carrying protein of red blood cells. Low levels produce anemia.

Human leukocyte antigen (HLA): molecules inside the macrophage, which binds to an antigenic peptide. Controlled by genes on the sixth chromosome. They can amplify or perpetuate certain immune and inflammatory responses.

Immune complex: an antibody and antigen together.

Immunosuppressant: a medication, such as cyclophosphamide or azathioprine, that suppresses the immune system.

La antibody: almost always seen with anti-SSA/anti-Ro, also called anti-SSB.

Leukopenia: a decrease in the number of white blood cells.

Livedo reticularis: a reddish or cyanotic pattern seen on arms, legs, and torso, especially in cold weather.

Nonsteroidal anti-inflammatory drug (NSAID): an agent that fights inflammation by blocking the actions of prostaglandin. Examples include aspirin, ibuprofen, and naproxen.

Pericarditis: inflammation of the pericardium (sac surrounding the heart).

Photosensitivity: sensitivity to ultraviolet light.

Pleuritis: irritation or inflammation of the lining of the lung.

Prednisone or prednisolone: synthetic steroids.

Proteinuria: excess protein levels in the urine (also called albuminuria).

Raynaud syndrome: discoloration of the hands or feet (blue, white, or red) especially with cold temperatures; a feature of an autoimmune disease. Also referred to as Raynaud's phenomenon.

Rheumatoid factor: autoantibodies that react with IgG; seen in most patients with rheumatoid arthritis and 25% of those with SLE.

Ro antibody: associated with Sjögren syndrome, sun sensitivity, neonatal lupus, and congenital heart block; also called anti-SSA.

Scleroderma: an autoimmune disease featuring rheumatoid-type inflammation, tight skin, and vascular problems.

Sedimentation rate: test that measures the precipitation of red cells in a column of blood; high rates usually indicate increased disease activity.

Serologic test for syphilis: a blood test revealing an antibody that may be found in patients with syphilis. It is falsely positive in 15% of patients with lupus. Associated with the lupus anticoagulant and antiphospholipid antibodies.

T cell: a lymphocyte responsible for immunologic memory.

Thrombocytopenia: low platelet count.

Vasculitis: inflammation of the blood vessels.

Source: [2; 3]

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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