Lupus

Goals & Objectives

Course Description

"Lupus" is an asynchronous online continuing education course for physical therapists and physical therapist assistants. This course presents updated information about Lupus including sections on symptomology, etiology, clinical manifestations, diagnosis, treatment, psychosocial aspects, and research.

Course Rationale

The purpose of this course is to present current information about Lupus. Physical therapists and physical therapist assistants. will find this information pertinent and useful when creating and implementing rehabilitation programs that address the challenges and needs specific to individuals with Lupus.

Course Goals and Objectives

Upon completion of this course, the participant will be able to:

1. differentiate between the various types of Lupus
2. identify demographic groups who are at high risk for Lupus
3. recognize the current theories relating to Lupus etiology
4. recognize how Lupus effects the various systems of the body
5. identify current mechanisms utilized to diagnose Lupus
6. identify all of the current treatment options available for Lupus
7. recognize the psychosocial effects that Lupus has on the patient and their family
8. identify the current research concerning Lupus
9. identify resources available for Lupus patients and their families

Course Provider – Innovative Educational Services

Course Instructor - Michael Niss, DPT

Target Audience - physical therapists and physical therapist assistants.

Course Educational Level – Introductory / intermediate

Course Prerequisites - None

Method of Instruction/Availability – Online text-based course available continuously.

Criteria for issuance of CE Credits - A score of 70% or greater on the course post-test.

Continuing Education Credits – 4 hours

Determination of Credits - Mergener Formula: .9 x [-22.3+(0.00209 x 88,932) + (2.78 x 20) + (15.5 x 3)] = 240 minutes = 4.0 hours

Fees - $39.95

Conflict of Interest – No conflict of interest exists for the presenter or provider of this course.

Refund Policy - Unrestricted 100% refund upon request. The request for a refund by the learner shall be honored in full without penalty or other consideration of any kind. The request for a refund may be made by the learner at any time without limitations before, during, or after course participation.

Lupus

Course Outline

Introduction

Lupus is a unique, complex disease with a wide scope of symptoms. It is also an elusive condition in that it affects individuals differently and often does not follow a predictable course. For example, a patient who appears to be in remission during a routine office visit can present at an emergency room the following week with severe pericarditis or sudden stroke.

A person diagnosed with lupus may have symptoms and disease activity that are easily managed with treatment, but it is not uncommon for health care professionals to encounter a lupus patient with numerous severe symptoms that are difficult to control. No two lupus cases are alike. As a result, care of the patient with lupus is a challenge that draws on all the resources, knowledge, and strengths the health care team has to offer. Each member of the health care team — physician, nurse, therapist, dietitian, social worker, and others — has an important role to play in treating specific aspects of the disease and in supporting the patient to cope with his or her condition.

Today, the prognosis for people with lupus is far brighter that it was even 20 years ago. Advances in research, improved treatments, a growing list of support networks and information resources, and an increased emphasis on close cooperation between the patient and her or his health care team mean that, for many patients, it is possible to have lupus yet remain active and involved with life, family, and work.

Defining Lupus

Lupus is one of many disorders of the immune system known as autoimmune diseases. In autoimmune diseases, the immune system turns against parts of the body it is designed to protect. This leads to inflammation and damage to various body tissues. Lupus can affect many parts of the body, including the joints, skin, kidneys, heart, lungs, blood vessels, and brain.
At present, there is no cure for lupus. However, lupus can be effectively treated with drugs, and most people with the disease can lead active, healthy lives. Lupus is characterized by periods of illness, called flares, and periods of wellness, or remission.

Types of Lupus

Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus (SLE) is the most common form of the disease, and the one that most people are referring to when they say "lupus." Lupus means “wolf.” Erythematosus means “redness.” In 1851, doctors coined this

name for the disease because they thought the facial rash that frequently accompanies lupus looked like the bite of a wolf.

In SLE, the body develops antibodies that react against the person's own normal tissue. This abnormal response leads to the many manifestations of SLE and can be very damaging. The course is unpredictable and individualized; no two patients are alike. Lupus is not contagious, infectious, or malignant. It usually develops in young women of childbearing years, but many men and children also develop lupus. African Americans and Hispanics have a higher frequency of this disease than do Caucasians. SLE also appears in the first-degree relatives of lupus patients more often than it does in the general population, which indicates a strong hereditary component. However, most cases of SLE occur sporadically, indicating that both genetic and environmental factors play a role in the development of the disease.

Lupus varies greatly in severity, from mild cases requiring minimal intervention to those in which significant and potentially fatal damage occurs to vital organs such as the lungs, heart, kidney, and brain. The disease is characterized by "flares" of activity interspersed with periods of improvement or remission. A flare, or exacerbation, is increased activity of the disease process with an increase in physical manifestations and/or abnormal laboratory test values. Periods of improvement may last weeks, months, or even years. The disease tends to remit over time. Some patients never develop severe complications, and the outlook is improving for those patients who do develop severe manifestations.

The symptoms of SLE may be mild or serious. Although SLE usually first affects people between the ages of 15 and 45 years, it can occur in childhood or later in life as well.

Discoid Lupus Erythematosus (DLE)

Discoid lupus erythematosus is a chronic skin disorder in which a red, raised rash appears on the face, scalp, or elsewhere. The raised areas may become thick and scaly and may cause scarring. The rash may last for days or years and may recur. It occurs in about 20% of patients with systemic lupus erythematosus. DLE only rarely progresses to systemic lupus erythematosus.

Drug-induced Lupus

Drug-induced lupus is a form of lupus caused by medications. Symptoms are similar to those of SLE (arthritis, rash, fever, and chest pain) and they typically go away completely when the drug is stopped. Many different drugs can cause drug-induced lupus. The clinical and serologic signs usually subside gradually after the offending drug is discontinued. A wide variety of drugs are implicated in this form of lupus.

Drugs Implicated as activators of lupus

Drugs with proven association

- Chlorpromazine
- Hydralazine
- Isoniazid
- Methyldopa
- Procainamide

Drugs with possible association

- Beta blockers (e.g., acebutolol, atenolol, labetalol, metoprotolol, oxprenolol, pindolol, practolol, and propranolol)
- Captopril
- Carbamazine
- Cimetidine
- Diphenylhydantoin (phenytoin)
- Ethosuximide

Neonatal Lupus

Neonatal lupus is a rare disease that can occur in newborn babies of women with SLE, Sjögren's syndrome, or no disease at all. Scientists suspect that neonatal lupus is caused by autoantibodies in the mother's blood called anti-Ro (SSA) and anti-La (SSB). At birth, the babies have a skin rash, liver problems, and low blood counts. These symptoms gradually go away over several months. In rare instances, babies with neonatal lupus may have a serious heart problem that slows down the natural rhythm of the heart. Neonatal lupus is rare, and most infants of mothers with SLE are entirely healthy. All women who are pregnant and known to have anti-Ro (SSA) or anti-La (SSB) antibodies should be monitored by echocardiograms (a test that monitors the heart and surrounding blood vessels) during the 16th and 30th weeks of pregnancy.

Demographics

Ninety percent of the people who have Lupus are women. African American women are three times more likely to get lupus than Caucasian women. It's also more common in Hispanic/Latino, Asian, and American Indian women.

Both African Americans and Hispanics/Latinos tend to develop lupus at a younger age and have more symptoms at diagnosis (including kidney problems).

They also tend to have more severe disease than whites. For example, African American patients have more seizures and strokes, while Hispanic/Latino

patients have more heart problems. It is not yet understood why some people seem to have more problems with lupus than others.

Lupus is most common in women between the ages of 15 and 44. These are roughly the years when most women are able to have babies. Scientists think a woman's hormones may have something to do with getting lupus. But it's important to remember that men and older people can get it, too.

It's less common for children under age 15 to have lupus. One exception is babies born to women with lupus. These children may have heart, liver, or skin problems caused by lupus. With good care, most women with lupus can have a normal pregnancy and a healthy baby.

Symptoms

General Manifestations of SLE

Fatigue is a nearly universal complaint of patients with SLE even when no other manifestations of the disease are present. The cause of this debilitating fatigue is not known. The patient should be evaluated for factors that may exacerbate fatigue, such as overexertion, insomnia, depression, stress, anemia, and other inflammatory diseases. Fatigue in SLE patients may be lessened by adequate rest, healthful diet, exercise, and attention to psychosocial factors.

Many patients with SLE experience changes in weight. At least one-half of patients report weight loss before being diagnosed with SLE. Weight loss in SLE patients may be attributed to a decreased appetite, side effects of medications, gastrointestinal problems, or fever. Weight gain can occur in some patients and may be due in part to prescribed medications, especially corticosteroids, or fluid retention from kidney disease.

Episodic fever is experienced by more than 80% of SLE patients, and there is no particular fever pattern. Although high fevers can occur during a lupus flare, low-grade fevers are more frequently seen. A complicating infection is often the cause of an elevated temperature in a patient with SLE. The patient’s WBC count may be normal to elevated with an infection, but low with SLE alone. However, certain medications, such as immunosuppressives, will suppress the WBC even in the presence of fever. Therefore, it is important to rule out other causes of a fever, including an infection or a drug reaction. Urinary and respiratory infections are common in SLE patients.

Psychological Manifestations

Psychological and emotional effects, such as grief, depression, and anger, are commonly experienced by lupus patients. These can be related to the outward changes, such as skin alterations, caused by the disease as well as by other

aspects of the disease and its treatment. It is important for health professionals to be alert to potential psychological repercussions and to assist in alleviating them.

Psychological Symptoms of Lupus

- Lowered self-esteem
- Negative feelings about body
- Decreased confidence
- Feelings of decreased self-worth
- Depression
- Feelings of sadness, hopelessness, helplessness. Difficulty in completing self-care activities, caring for children, maintaining a household, and other activities of daily living (ADL)
- Inability to maintain full- or part-time employment
- Decreased social activities
- Lack of energy or ambition
- Irritability
- Impaired concentration
- Crying
- Insomnia
- Suicidal thoughts

Dermatologic Manifestations

Approximately 80% of patients with SLE have skin manifestations and often suffer from itching, pain, and disfigurement. The classic sign of SLE is the “butterfly” rash extending over the cheeks (malar area) and bridge of the nose. This rash ranges from a faint blush to a severe eruption with scaling. It is photosensitive, and it may be transitory or fixed. Between 55 and 85% of patients develop this rash at some time in the course of the disease.

Other rashes may occur elsewhere on the face and ears, upper arms, shoulders, chest, and hands. DLE is seen in 15–30% of patients with SLE. Subacute cutaneous LE, seen in about 10% of SLE patients, produces highly photosensitive papules that itch and burn. Skin changes, especially the butterfly rash and subacute cutaneous LE, can be precipitated by sunlight.

Some patients may develop mouth, vaginal, or nasal ulcers. Hair loss (alopecia) occurs in about one-half of SLE patients. Most hair loss is diffuse, but it may be patchy. It can be scarring or nonscarring. Alopecia may also be caused by corticosteroids, infection, or immunosuppressive drugs.

Raynaud’s phenomenon (paroxysmal vasospasm of the fingers and toes) frequently occurs in patients with SLE. For most patients, Raynaud’s phenomenon is mild. However, some SLE patients with severe Raynaud’s phenomenon may develop painful skin ulcers or gangrene on the fingers or toes.

Varying levels of pain and discomfort due to skin alterations may occur. Pruritus accompanies many types of skin lesions.

Skin alterations in the lupus patient, particularly those of DLE, can be disfiguring. As a result, patients may experience fear of rejection by others, negative feelings about their body, and depression. Changes in lifestyle and social involvement may occur.

Dermatologic Symptoms of Lupus

- Butterfly rash on cheeks and bridge of nose
- Scaly, disk-shaped scarring rash (DLE)
- Erythematous, slightly scaly papules (subacute cutaneous LE)
- Psoriasiform or arcuate (curved) lesions on the trunk of the body (subacute cutaneous LE)
- Itching and burning
- Ulcers in the mouth, vagina, or nasal septum
- Atrophy (including striae or stretch marks)
- Impaired wound healing
- Easy bruising
- Petechiae
- Increased body hair (hirsutism)
- Steroid-induced ecchymosis
- Ulcers or gangrene on fingers or toes (Raynaud's Phenomenon)
- Alopecia

Musculoskeletal Manifestations

Arthralgia or arthritis is experienced by 95% of SLE patients at some time during the course of the disease. Articular pain is the initial symptom in about one-half of patients eventually diagnosed with SLE. Morning stiffness and joint and muscle aching can also occur. Joint pain is typically migratory and symmetric (but may be asymmetric in some patients). Joints may become warm and swollen. X rays of the joints usually do not show erosion or destruction of bone.

Unlike rheumatoid arthritis, the arthritis of SLE tends to be transitory. Proliferation of the synovium is more limited, and joint destruction is rare. The joints most commonly involved are those of the fingers, wrists, and knees; less commonly involved are the elbows, ankles, and shoulders.

Several joint complications may occur in SLE patients, including Jaccoud's arthropathy and osteonecrosis. Subcutaneous nodules, especially in the small joints of the hands, are seen in about 5% of patients. Tendinitis, tendon rupture, and carpal tunnel syndrome are seen.

Musculoskeletal Symptoms of Lupus

- Morning stiffness and aching

- Joint pain
- Warm, swollen joints
- Ulnar deviation of the fingers with swan neck deformities and subluxations
- Generalized myalgia and muscle tenderness, especially in the upper arms and upper legs

Hematologic Manifestations

Abnormal blood conditions are common in patients with SLE. Problems include anemia, thrombocytopenia, and other clotting disorders.

Anemia, which is common in SLE patients, reflects insufficient bone marrow activity, shortened RBC life span, or poor iron uptake. Aspirin, NSAIDs, and prednisone can cause stomach bleeding and exacerbate the condition. There is no specific therapy for this type of anemia. Immune-mediated anemia (or hemolytic anemia), which is due to antibodies directed at RBCs, is treated with corticosteroids.

Thrombocytopenia may occur and may respond to low-dose corticosteroids. Mild forms may not need to be treated, but a severe form requires high-dose corticosteroid or cytotoxic drugs. The major clinical features of APLs and APL syndrome are venous thrombosis, arterial thrombosis, and thrombocytopenia with a history of positive anticardiolipin antibody (ACL) tests.

Abnormal laboratory tests may often include a false-positive VDRL test for syphilis. Fluorescent treponemal antibody absorption (FTA-ABS) and microhemagglutination-*Treponema pallidum* (MHA-TP) tests, which are more specific tests for syphilis, are almost always negative if the patient does not have syphilis. An elevated erythrocyte sedimentation rate (ESR) is a common finding in active SLE, but it does not always mirror disease activity.

Hematologic Symptoms of Lupus

Anemia

- Decreased hemoglobin and hematocrit values
- Positive Coombs' test (hemolytic anemia)
- Tachycardia
- Palpitations
- Dizziness
- Sensitivity to cold
- Chronic fatigue, lethargy, and malaise
- Pallor
- Weakness
- Dyspnea on exertion
- Headache

Thrombocytopenia

- Petechiae
- Excessive bruising of skin
- Bleeding from gums, nose
- Blood in stool

Cardiopulmonary Manifestations

Cardiac abnormalities contribute significantly to morbidity and mortality in SLE and are one of the most important clinical manifestations of the disease. In addition, involvement of the lungs and pleurae is common. Pericarditis, an inflammation of the pericardium, is the most common cardiac abnormality in SLE. Myocarditis, an inflammation of the heart muscle, may also occur, but is rare. Myocardial infarction, caused by atherosclerosis, has been reported in SLE patients below the age of 35 years.

Vasculitis (inflammation of the blood vessels) and serositis (inflammation of serous membranes) are frequently part of the autoimmune pathology of SLE. These conditions respond well to corticosteroids. Vasculitis may cause many different symptoms, depending on the system(s) most affected. Serositis most commonly presents as pleurisy or pericarditis. Pleuritic chest pain is common. Pleurisy is the most common respiratory manifestation in SLE. Attacks of pleuritic pain can also be associated with pleural effusions. Many patients complain of chest pain, but pericardial changes are not often demonstrated on clinical evaluation.

Cardiopulmonary Symptoms of Lupus

Pericarditis

- Pain in the anterior chest, neck, back, or arms that is often relieved by sitting up
- Shortness of breath
- Swelling of legs and feet
- Fever
- Chills
- Audible pericardial friction rub

Myocarditis

- Chest pain
- Shortness of breath
- Fever
- Fatigue
- Palpitations

Atherosclerosis Leading to Myocardial Infarction
- Burning, choking, squeezing, or pressing chest pain that may radiate to left shoulder and arm
- Shortness of breath
- Weakness
- Unrelieved indigestion
- Nausea and vomiting

Pleurisy
- Shortness of breath
- Chest pain, especially with deep inspiration
- Coughing up blood or thick mucus

Periungual Erythema
- Redness in the nailbed

Livedo Reticularis
- A reddish or cyanotic pattern seen on arms, legs, torso, especially in cold weather

Leukocytoclastic Vasculitis
- Necrotic ulcerations, including raised hemorrhagic nodules (papule, purpura) that ulcerate, especially on the lower legs, ankles, and dorsa of the feet

Venous Thrombosis
- Positive Homans' sign
- Pain, swelling, inflammation, redness, and warmth in the affected limb
- Increased circumference of affected limb

Arterial Thrombosis
- Pain or loss of sensation due to ischemia
- Panesthesias and loss of position sense
- Coldness
- Pallor
- Paralysis
- No pulse

Renal Manifestations

Renal damage is one of the most serious complications of SLE. The majority of lupus patients have some degree of asymptomatic microscopic kidney damage. Less than 50% have clinical renal disease, and most of those with renal disease

have one of the milder forms. Kidney damage may necessitate treatment with corticosteroids, cytotoxic agents, dialysis, or renal transplantation.

Renal biopsy can be helpful in making decisions about drug treatments and determining prognosis by assessing the presence of active renal disease versus scarring.

Renal Symptoms of Lupus

SLE Nephropathy

- Hematuria (as few as 5 RBCs is significant)
- Proteinuria (>1+ to 2+)
- Abacterial pyuria
- Elevated creatinine level (indicates loss of renal function)
- Elevated blood urea nitrogen (BUN)
- Markedly abnormal serologic tests, such as decreased complement or elevated anti-DNA values
- Weight gain
- Ankle edema
- Hypertension

Renal Failure

- Nausea and vomiting
- Anorexia
- Anemia
- Lethargy
- Pruritus
- Changing level of consciousness

Fluid and Electrolyte Imbalance

- Weight gain
- Pitting edema of the lower extremities
- Sacral edema
- Bounding pulse, elevated blood pressure, S3 gallop
- Engorgement of neck and hand veins
- Dyspnea
- Constant cough
- Crackles in lungs
- Cyanosis
- Decreased hematocrit
- Urine specific gravity <1.010
- Variable serum sodium level (normal, high, or low), depending on the amount of sodium retention or water retention
- Serum osmolality <275 mOsm/kg

Urinary Tract Infection

- Dysuria / frequent urination
- Urgent need to urinate
- Fever
- Cloudy urine
- Incomplete emptying of the bladder
- Low back or suprapubic pain
- Flank pain
- Malaise
- Nausea and vomiting

Central Nervous System Manifestations

Neurologic manifestations of SLE are common and vary from mild to severe. They can be difficult to diagnose and distinguish from other diseases. All portions of the nervous system may be affected, including the CNS. Definite diagnosis of CNS lupus may be difficult, as symptoms may be related to medications, other medical conditions, or to individual reactions to chronic illness.

Cranial or peripheral neuropathy occurs in 10–15% of patients; it is probably secondary to vasculitis in small arteries supplying nerves. Cerebrovascular accidents are reported in approximately 15% of patients. Between 10 and 20% of patients experience seizures. Although cognitive impairment is believed to be very common, there are few measurements to document it.

Serious CNS involvement ranks behind only kidney disease and infection as a leading cause of death in lupus. However, the majority of SLE patients with CNS complications do not develop a life-threatening disease.

CNS Symptoms of Lupus

General CNS lupus

- Headaches
- Fever
- Confusion
- Seizures
- Psychosis

Cranial neuropathies

- Visual defects
- Blindness
- Nystagmus
- Ptosis
- Papilledema (edema in the optic disk)
- Tinnitus
- Vertigo
- Facial palsy

Cognitive impairment

- Confusion
- Impaired long- and short-term memory
- Difficulty in conceptualizing, abstracting, generalizing, organizing, and planning information for problem solving
- Difficulties in personal and extrapersonal orientation
- Altered visual-spatial abilities
- Selective attention
- Difficulties in pattern recognition, sound discrimination and analysis, and visual-motor integration

Mental changes

- Depression
- Anxiety
- Affective disorder
- Mood swings
- Hypomania or mania (especially with corticosteroid use)

Gastrointestinal Manifestations

Gastrointestinal (GI) problems are common and range from vague complaints of anorexia to life-threatening bowel perforation secondary to mesenteric arteritis. Anorexia, nausea, vomiting, and diarrhea may be related to the use of salicylates, NSAIDs, antimalarials, corticosteroids, and cytotoxic drugs.

SLE patients who present with acute abdominal pain and tenderness need immediate, aggressive, and comprehensive evaluation to rule out an intra-abdominal crisis. Ascites, an abnormal accumulation of fluid in the peritoneal cavity, is found in about 10% of SLE patients. Pancreatitis is a serious complication occurring in approximately 5% of SLE patients and is usually secondary to vasculitis.

Mesenteric or intestinal vasculitis are life-threatening conditions that may have complications of obstruction, perforation, or infarction. They are seen in more than 5% of patients with SLE. Abnormal liver enzyme levels are also found in about one-half of SLE patients (usually secondary to medications). Active liver disease is rarely found.

GI Symptoms of Lupus

General manifestations

- Persistent sore throat
- Dry mouth (characteristic of patients with coexisting Sjögren's syndrome)
- Anorexia
- Nausea and vomiting

- Diarrhea
- Dysphagia (especially in association with Raynaud's phenomenon)

Pancreatitis

- Mild nonspecific abdominal pain to severe epigastric pain radiating to the back
- Nausea
- Vomiting
- Elevated serum amylase level
- Dehydration

Ascites

- Abdominal distention
- Bulging flanks
- Downward protruding umbilicus

Mesenteric and intestinal vasculitis

- Cramping or constant abdominal pain
- Vomiting
- Fever
- Diffuse direct and rebound abdominal tenderness

Ophthalmologic Manifestations

Visual impairment may be due to SLE or to drug treatment (corticosteroids or antimalarials), or it may be a separate problem (glaucoma or retinal detachment). Blindness due to SLE occurs, but is rare. Other visual problems may occur:

A lupus rash may develop on the eyelids.

Conjunctivitis occurs in 10% of SLE patients and is usually infectious. Kerato-conjunctivitis is usually mild.

Cytoid bodies are the most common retinal change in SLE. They reflect microangiopathy of the retinal capillaries and localized microinfarction of the superficial nerve fiber layers of the retina.

Sjögren's syndrome is an autoimmune condition manifest as excessive dryness of mucous membranes. Lupus patients with these symptoms require artificial tears to relieve dry eyes.

Glaucoma and cataracts may be caused by corticosteroids.

Antimalarials can damage the retina, which can impair vision (particularly color vision) or, rarely, cause blindness.

Ophthalmologic Symptoms of Lupus

- A lupus rash on the eyelids
- Red, sore, swollen eyes
- Tearing
- Mucus discharge from eyes, particularly upon awakening
- Sensitivity to light
- Change in vision
- Blurred vision
- Cloudy lens(es)
- Dry eyes
- Burning sensation in eyes

Infection

SLE affects the immune system, thus reducing the body's ability to prevent and fight infection. In addition, many of the drugs used to treat SLE also suppress the function of the immune system, thereby further depressing the ability to fight infection. The risk of infection parallels medication dosages and duration of treatment.

Patients with SLE who show signs and symptoms of infection need prompt therapy to prevent it from becoming life threatening. The most common infections involve the respiratory tract, urinary tract, and skin and do not require hospitalization if they are treated promptly. Other opportunistic infections, particularly Salmonella, herpes zoster, and Candida infections, are more common in patients with SLE because of altered immune status.

Infection Symptoms of Lupus

Respiratory tract infections

- Sore throat
- Sneezing
- Fever
- Productive or nonproductive cough
- Runny nose
- Malaise
- Chills
- Back and muscle pain
- Dyspnea
- Wheezing or rales
- Chills
- Nausea
- Vomiting

Urinary tract infections

- Chills

- Fever
- Flank pain
- Vomiting
- Urinary frequency
- Dysuria
- Hematuria

Skin infections

- Lesions
- Redness
- Swelling
- Tenderness or pain

Nutritional Disorders

The patient with lupus often has special nutritional problems related to medical conditions that may arise during the course of the disease. Potential problems include weight changes, anorexia, and nutritional deficiencies and hypertoxicities secondary to drug therapies.

Nutritional Disorder Symptoms of Lupus

- Weight loss or gain
- Loss of interest in food
- Anorexia
- Dry, rough, scaly skin
- Dull, dry, brittle, thin hair
- Loss of lean muscle mass
- Listlessness, apathy
- Poor muscle tone
- Constipation or diarrhea
- Irritability
- Fatigue and lack of energy
- Inflamed or bleeding gums

Etiology

Lupus is a complex disease, and its cause is unknown. It is likely that a combination of genetic, environmental, and possibly hormonal factors work together to cause the disease.

Investigators have found evidence to support several likely possibilities in the etiology of SLE. Some believe there may be more than one type of SLE and that its etiology may vary from one person to the next. Current studies are focusing on the following elements:

- immune system dysfunction
- genetics
- environmental influences
- hormones

Immune System Dysfunction

Lupus is an autoimmune disease, so called because a person's immune system attacks her or his own tissues. In lupus, the signs and symptoms of the disease can be attributed to damage caused directly by antibodies, the deposition of immune complexes (the combination of antigen and antibody), or cell-mediated immune mechanisms. A number of steps are involved in these mechanisms, and scientists hope to reveal the cause of lupus by examining each step. In the process of doing so, they also may find new ways to treat lupus.

One of the hallmarks of lupus is the formation of autoantibodies, which are antibodies that react with a person's own tissue. Autoantibodies occasionally can be present in healthy people, but they are typically found in low concentrations. Essentially all patients with lupus have autoantibodies, generally in high concentrations. The autoantibodies found in lupus patients are often called antinuclear antibodies because they generally target the nucleic acids, proteins, and ribonucleoprotein complexes inside a cell's nucleus. Other autoantibodies in lupus patients also can bind to cell surface membranes and destroy cells directly.

Research studies have shown an association between the presence of certain autoantibodies and particular manifestations of lupus, such as kidney or skin disease. Scientists are now trying to establish whether these autoantibodies actually cause signs or symptoms of lupus. However, most people with lupus test positive for many different autoantibodies, so it is often very difficult to identify which autoantibodies are responsible for a specific type of tissue damage in human subjects.

In lupus, the immune system produces too many autoantibodies and forms too many immune complexes. Normally, antigen-antibody immune complexes are joined by complement, a substance in the blood that aids in the breakup and removal of immune complexes from the body. Scientists have found that SLE patients have both inherited and acquired abnormalities in complement and complement receptors. These deficiencies in complement may decrease the body's ability to get rid of immune complexes. Immune complexes not broken up may be deposited in various body tissues, leading to the inflammation that causes tissue damage.

Genetics

There is considerable evidence showing that genes play a role in the etiology of lupus. The extremely high occurrence of lupus in identical twins and the

increased prevalence of lupus among first- and second-degree relatives of lupus patients suggests a genetic component. In addition, when researchers look at autoantibodies typically found in a lupus patient and her or his siblings and compare them with clinical manifestations of the disease in the individuals, they find that the individuals have the autoantibodies in common more often than they have the clinical manifestations in common. This finding indicates a genetic basis for the formation of autoantibodies that play a role in lupus.

Studies to date suggest that many different genes contribute to lupus susceptibility and that no single genetic abnormality causes the disease. It also appears that genes may be influential in determining the type or severity of lupus. For example, among African Americans with lupus, those with lupus nephritis are more likely than those with other clinical manifestations to have the gene for a form of a receptor that has a low efficiency for capturing immune complexes.

Other genes that have been associated with lupus in humans include

- the immune system genes human leukocyte antigen HLA-DR3, HLA-DR2, and complement C4 genes;
- alleles at HLA-DR and HLA-DQ, which are associated with certain autoimmune characteristics found in lupus; and
- a polymorphism of the T-cell receptor, which has been associated with anti-Ro, one of the autoantibodies commonly found in mothers of babies with neonatal lupus erythematosus.

Researchers studying lupus in animals have recently discovered a single gene that causes a lupus-like illness in mice. In these mice, the fas gene, one of the genes that controls apoptosis (programmed cell death), is defective. When the defective fas gene is replaced with a normal gene, the mice no longer develop signs of the disease.

Scientists continue to study the genetics of lupus in humans and in animals. If the genes that create a genetic predisposition for lupus can be identified, it may be feasible to correct genetic defects through gene therapy or other treatments.

Environmental Influences

Researchers believe that genetic predisposition is just one piece of the puzzle of lupus etiology. Studies have shown that the occurrence of lupus is high among both members of a pair of identical twins and much lower among nonidentical twins and other full siblings. The fact that this concordance is not 100% among identical twins, however, suggests that environmental agents probably trigger lupus in individuals with a genetic predisposition. Environmental factors that scientists are considering include sunlight, stress, certain chemical substances, and infectious agents such as viruses.

Sunlight
Exposure to the UV rays of sunlight can lead to a skin rash and exacerbate systemic manifestations of lupus. Exposure to UVB light causes certain cellular proteins to accumulate in abnormally large amounts on the cell's surface. These proteins react with autoantibodies commonly found in people with SLE, leading to a local or systemic inflammatory response.

Stress
Doctors suspect stress is a possible trigger for lupus flares. Frequently, patients ascribe their first symptoms or worsening symptoms to a stressful event, such as divorce, death of a loved one, or job loss. Scientists do not have a clear explanation for this phenomenon, but research is being done to find out whether stress hormones such as adrenaline or cortisone may influence the development or course of the disease.

Chemical Substances
A number of drugs cause a lupus-like illness in susceptible individuals, including chlorpromazine, hydralazine, isoniazid, methyldopa, and procainamide. When the offending drug is stopped, the lupus symptoms resolve. When researchers determine how these drugs cause lupus, they may be able to provide further answers on the etiology of SLE.

Viruses
Many researchers suspect that infectious agents, such as viruses, may trigger lupus, somehow disrupting cellular immune function in susceptible individuals. It is possible that the virus infects B cells (cells programmed to produce antibodies in response to specific antigens) and causes them to produce autoantibodies. Researchers are studying various mechanisms by which viruses could result in autoimmunity.

Hormones

SLE is more prevalent in women during their reproductive years. In addition, disease activity sometimes flares during pregnancy or during the postpartum period. For these reasons, researchers have long considered that hormones may influence lupus. Some research in animals also supports this supposition. Lupus-like illnesses in animals are exacerbated when they receive female hormones. Studies are under way to find out more about how hormones may influence the course and development of lupus.

Pregnancy and Lupus

Twenty years ago, women with lupus were counseled not to become pregnant because of the risk of a flare of the disease and an increased risk of miscarriage. Research and careful treatment have made it possible for more and more women

with lupus to have successful pregnancies. Although a lupus pregnancy is still considered high risk, most women with lupus are able to carry their babies safely to term. Approximately 20–25% of lupus pregnancies end in miscarriage, compared with 10–15% of pregnancies in women without the disease. Pregnancy counseling and planning before pregnancy is important. Optimally, a woman should have no signs or symptoms of lupus before she becomes pregnant.

Researchers have now identified two closely related lupus autoantibodies, anticardiolipin antibody and lupus anticoagulant, that are associated with risk of miscarriage. One-third to one-half of women with lupus have these autoantibodies, which can be detected by blood tests. Identifying women with the autoantibodies early in the pregnancy may help physicians take steps to reduce the risk of miscarriage. Pregnant women who test positive for these autoantibodies and who have had previous miscarriages are generally treated with baby aspirin or heparin throughout their pregnancy.

Some women may experience a mild to moderate flare during or after their pregnancy; others may not. Pregnant women with lupus, especially those taking corticosteroids, are also likely to develop pregnancy-induced hypertension, diabetes, hyperglycemia, and kidney complications. About 25% of babies of women with lupus are born prematurely, but do not suffer from birth defects.

About 3% of babies born to mothers with SLE will have neonatal lupus, or specific antibodies called anti-Ro(SSA) and anti-La(SSB). This is not the same as SLE and is almost always temporary. The syndrome is thought to be caused by passive transfer of anti-Ro antibodies from the mother to the fetus. About one-third of women with SLE have this antibody. By 3–6 months of age, the rash and blood abnormalities associated with neonatal lupus disappear. Very rarely, babies with neonatal lupus will have a congenital complete heart block. This problem is permanent, but can be treated with a pacemaker.

Diagnosis

The onset of lupus may be acute, resembling an infectious process, or it may be a progression of vague symptoms over several years. As a result, diagnosing SLE is often a challenge. A consistent, thorough medical examination by a doctor familiar with lupus is essential to an accurate diagnosis. This must include a complete medical history and physical examination, laboratory tests, and a period of observation (possibly years). The doctor, nurse, or other health professional assessing a patient for lupus must keep an open mind about the varied and seemingly unrelated symptoms that the patient may describe. For example, a careful medical history may show that sun exposure, use of certain drugs, viral disease, stress, or pregnancy aggravates symptoms, providing a vital diagnostic clue.

No single laboratory test can definitely prove or disprove SLE. Initial screening includes a complete blood count (CBC), liver and kidney screening panels, laboratory tests for specific autoantibodies (e.g., antinuclear antibodies [ANA]), a syphilis test (VDRL), urinalysis, blood chemistries, and erythrocyte sedimentation rate (ESR). Abnormalities in these test results will guide further evaluations. High-titer anti-nDNA antibody or anti-Sm antibody are important indications of lupus. Specific immunologic studies, such as those of complement components (e.g., C3 and C4) and other autoantibodies (e.g., anti-La and anti-Ro), are used to help evaluate the patient's immune status and to monitor the activity of the disease. At times, biopsies of the skin or kidney using immunofluorescent staining techniques can support a diagnosis of SLE. A variety of laboratory tests, X rays, and other diagnostic tools are used to rule out other pathologic conditions and to determine the involvement of specific organs. It is important to note, however, that any single test may not be sensitive enough to reflect the intensity of the patient's symptoms or the extent of the disease's manifestations.

The American College of Rheumatology (ACR), has developed and refined a set of 11 diagnostic criteria. If at least 4 of the 11 criteria develop at one time or individually over any period of observation, then the patient is likely to have SLE. However, a diagnosis of SLE can be made in a patient having fewer than four of these symptoms.

ACR Criteria for Diagnosing SLE

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcers
- Arthritis
- Serositis (pleuritis or pericarditis)
- Renal disorder (persistent proteinuria or cellular casts)
- Neurological disorder (seizures or psychosis)
- Hematologic disorder (anemia, leukopenia or lymphopenia on two or more occasions, thrombocytopenia)
- Immunologic disorder (positive LE cell preparation, abnormal anti-DNA or anti-Sm values, false-positive VDRL syphilis test)
- Abnormal ANA titer

Tests for Blood Cell Abnormalities

Blood cell abnormalities often accompany SLE. People suspected of having lupus are usually tested for anemia, leukopenia, and thrombocytopenia.

Anemia

Tests for anemia include those for hemoglobin, hematocrit, and red blood cell (RBC) count. In addition, the levels of iron, total iron-binding capacity, and ferritin

may be tested. At any time during the course of the disease, about 40% of patients with SLE will be anemic. The anemia may be caused by iron deficiency, GI bleeding, medications, or autoantibody formation to RBCs. When first diagnosed, about 50% of patients have a form of anemia in which the concentration of hemoglobin and the size of the RBCs are normal. This is called normochromic- normocytic anemia, or “anemia of chronic disease.” Autoimmune hemolytic anemia, with a positive Coombs test, is much less common.

Leukopenia and Thrombocytopenia
Abnormalities in the white blood cell (WBC) and platelet counts are an important indicator of SLE. Leukopenia, a decrease in the number of WBCs, is very common in active SLE and is found in 15–20% of patients. Thrombocytopenia, or a low platelet count, occurs in 25–35% of patients with SLE.

Measurements of Autoimmunity

The presence of certain autoantibodies has diagnostic value for SLE. The most specific tests are those that detect high levels of these autoantibodies. The most common and specific tests for autoantibodies and other elements of the immune system are listed first.

Antinuclear Antibody (ANA)
A screening test for ANA is standard in assessing SLE because it is positive in close to 100% of patients with active SLE. However, it is also positive in 95% of patients with mixed connective tissue disease, in more than 90% of patients with systemic sclerosis, in 70% of patients with primary Sjögren’s syndrome, in 40–50% of patients with rheumatoid arthritis, and in 5–10% of patients with no systemic rheumatic disease. Patients with SLE tend to have high titers of ANA. False-positive results are found during chronic infectious diseases, such as subacute bacterial endocarditis, tuberculosis, hepatitis, and malaria. The sensitivity and specificity of ANA determinations depend on the technique used.

Anti-Sm
Anti-Sm is an immunoglobulin specific against Sm, a ribonucleoprotein found in the cell nucleus. This test is highly specific for SLE; it is rarely found in patients with other rheumatic diseases. However, only 30% of patients with SLE have a positive anti-Sm test.

Anti-nDNA
Anti-nDNA is an immunoglobulin specific against native (double-stranded) DNA. This test is highly specific for SLE; it is not found in patients with other rheumatic diseases. Sixty to eighty percent of patients with active SLE have a positive anti-nDNA test. For many patients with anti-nDNA, the titer is a useful measure of disease activity. The presence of anti-nDNA is associated with a greater risk of lupus nephritis.

Anti-Ro(SSA) and Anti-La(SSB)
These immunoglobulins, commonly found together, are specific against RNA proteins. Anti-Ro is found in 30% of SLE patients and 70% of patients with primary Sjögren's syndrome. Anti-La is found in 15% of lupus patients and 60% of patients with primary Sjögren's syndrome. Anti-Ro is highly associated with photosensitivity; both are associated with neonatal lupus.

Complement
Complement proteins constitute a serum enzyme system that helps mediate inflammation. Complement components are triggered into an activated form by such immunologic events as interaction with immune complexes. Complement components are identified by numbers (C1, C2, etc.). Genetic deficiencies of C1q, C2, and C4, although rare, are commonly associated with SLE. A test to evaluate the entire complement system is called CH50. The most commonly measured complement components are the serum level of C3 and C4. These tests are particularly useful in evaluating kidney involvement and in monitoring the disease over time.

Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP)
Tests for ESR and CRP are nonspecific tests to detect generalized inflammation. Levels are generally increased in patients with active lupus and decline when corticosteroids or NSAIDs are used to reduce inflammation.

Antiphospholipid Antibodies (APLs)
APLs are autoantibodies that react with phospholipids. Recent data indicate that APLs recognize a number of phospholipid-binding plasma proteins (e.g., prothrombin, ß2-glycoprotein I) or protein-phospholipid complexes rather than phospholipids alone. APLs are present in 30–40% of lupus patients. A positive APL test plus the presence of arterial and venous thrombosis and thrombo-embolism or recurrent fetal deaths or thrombocytopenia is called APL syndrome. APL syndrome affects about a third of lupus patients with APLs (10–15% of all lupus patients). APLs and APL syndrome may also occur in patients without lupus (primary APL syndrome). APLs are detected in the following three types of laboratory assays.

Syphilis Serology
Certain blood tests for syphilis are often falsely positive in lupus patients. Chronically false-positive VDRL or rapid plasma reagin (RPR) tests frequently occur in patients with lupus. Cardiolipin, a phospholipid, is a component of the antigenic mixture used in these assays. More specific tests for syphilis, such as the fluorescent treponemal antibody-absorbed (FTA-ABS) and microhemagglutination-*Treponema pallidum* (MHA-TP) assays, are almost always negative in lupus patients without syphilis.

Anticardiolipin Antibody (ACA)
Sensitive enzyme-linked immunoabsorbent assays (ELISA) using cardiolipin as

the putative antigen are commonly used to detect APLs. In patients with APL syndrome, most antibodies detected in anticardiolipin ELISAs are directed against cardiolipin-bound ß2-glycoprotein I.

Lupus Anticoagulant

Lupus anticoagulants are APLs that inhibit certain coagulation tests, such as the activated partial thromboplastin time (aPTT), dilute Russell viper venom time (dRVVT), and kaolin clotting time (KCT). Although the antibodies act as anticoagulants in these laboratory assays, they are not clinically associated with hemorrhage, but with thrombosis and other manifestations of the APL syndrome. Most lupus anticoagulant antibodies are directed against prothrombin or ß2-glycoprotein I.

Tests for Kidney Disease

Several tests can be done to assess a patient for kidney disease.

Measurement of Glomerular Filtration Rate

The glomerular filtration rate is a measure of the efficiency of kidneys in filtering blood to excrete metabolic products. Typically, this is done by collecting a 24-hour urine sample for measurement of creatinine clearance. Impairment of renal function by lupus nephritis results in reduced levels of creatinine clearances.

Urinalysis

Urinalysis can indicate the presence or extent of renal disease. For example, proteinuria can be a reliable indicator of renal disease. The presence of RBCs, WBCs, and cellular casts, particularly red cell casts, in the urine also indicates renal disease.

Measurement of Serum Creatinine Concentration

Creatinine is a waste product of muscle metabolism that is excreted by the kidney. Loss of renal function as a consequence of lupus nephritis causes increases in serum levels of creatinine. The concentration of creatinine in the serum can be used to assess the degree of renal impairment.

Kidney Biopsy

Kidney biopsy can be used to determine the presence of immune complexes and the presence, extent, and type of inflammation in the glomeruli. Diagnosis of the extent and type of inflammation may help to determine a treatment program for lupus.

Treatment

Diagnosing and treating lupus are often a team effort between the patient and several types of health care professionals. A person with lupus can go to his or

her family doctor or internist, or can visit a rheumatologist. Clinical immunologists may also treat people with lupus. As treatment progresses, other professionals often help. These may include nurses, psychologists, social workers, physical therapists, occupational therapists, nephrologists, hematologists, dermatologists, and neurologists.

The treatment of SLE is as varied as its course. Although there is no cure for lupus and it is difficult to predict which treatment will be most effective for each patient, there have been significant gains in treating patients, and there is general consensus on several treatments.

A conservative regimen of physical and emotional rest, protection from direct sunlight, a healthful diet, prompt treatment of infections, and avoidance of known allergens and aggravating factors are the mainstays of lupus therapy. In addition, for female patients, pregnancy must be planned for times when the disease is in remission.

Physical Rest
This basic component of everyone's good health is essential for the lupus patient. The fatigue of lupus is not sleepiness or tiredness from physical exertion, but rather a frequent, persistent complaint often described as a "bone-tired feeling" or a "paralyzing fatigue." Normal rest often does not refresh the patient or eliminate the tiredness due to lupus, and fatigue may persist despite normal laboratory test results. The patient and family need instruction on how to use this tiredness as a guide to activity and when the person should stop for rest. It must be reinforced that this need for rest is not laziness. Restful sleep of 8–10 hours per night, naps, and "timeouts" during the day are basic guidelines; strict bed rest is usually not required. Physical activity should be encouraged as the patient can tolerate it. An individualized exercise routine may facilitate recovery from a flare and promote well-being.

Emotional Rest
A patient's emotional stressors should be carefully assessed, because they may play a role in triggering a flare. The patient should be instructed on how to avoid these stressful situations. However, the physical manifestations of lupus must be treated as they present themselves while the emotional stresses are explored. Discussions with the family on this issue are essential for providing information and in obtaining their support. Counseling for both the patient and the family may be an option.

Protection from Direct Sunlight
Photosensitivity is an abnormal reaction to the ultraviolet (UV) rays of the sun and results in the development or exacerbation of a rash that is sometimes accompanied by systemic symptoms. About one-third of lupus patients are photosensitive. All lupus patients should avoid direct, prolonged exposure to the sun. Sun-sensitive patients should frequently apply a sunscreen with a Sun

Protection Factor (SPF) of at least 15, avoid unprotected exposure between 10 a.m. and 4 p.m., and wear protective clothing, such as wide-brimmed hats and long sleeves. Lupus patients should be aware that UV rays are reflected off water and snow, and that glass, such as car windows, does not provide total protection from UV rays.

Lupus patients should also know that fluorescent and halogen lights may emit UV rays and can aggravate lupus. This may be an issue for patients who work in offices lit by these kinds of lights. Sunscreen and protective clothing can help minimize exposure, and plastic devices are available that block UV emissions from fluorescent or halogen light bulbs.

Diet and Nutrition

The patient with lupus often has special nutritional needs related to medical conditions that may arise during the course of the disease. These conditions include steroid-induced osteoporosis or diabetes, cardiovascular disease, and kidney disease. For the SLE patient to maintain optimal health, the therapist must work closely with the patient, dietitian, and physician to develop a nutritional plan specific to the patient's disease and manifestations.

A well-balanced diet is essential in maintaining good health for all people, including lupus patients. There are currently no specific dietary recommendations or limitations for those with lupus, but a restricted diet plan may be prescribed when fluid retention, hypertension, kidney disease, or other problems are present. Food intolerances and allergies may occur, but there is no evidence that these are more common in lupus patients than in the general population. The health professional should make a note of the patient's dietary history and suggest diet counseling if appropriate, especially if the patient has a problem with weight gain, weight loss, gastrointestinal (GI) distress, or food intolerances.

Fighting Infections

SLE affects the immune system, thus reducing the body's ability to prevent and fight infection. In addition, many of the drugs used to treat SLE also suppress the function of the immune system, thereby further depressing the ability to fight infection. The risk of infection parallels medication dosages and duration of treatment.

Patients with SLE who show signs and symptoms of infection need prompt therapy to prevent it from becoming life threatening. The most common infections involve the respiratory tract, urinary tract, and skin and do not require hospitalization if they are treated promptly. Other opportunistic infections, particularly Salmonella, herpes zoster, and Candida infections, are more common in patients with SLE because of altered immune status.

Prompt recognition and treatment of infection is essential for those with lupus. However, cardinal signs of infection may be masked because of SLE treatments.

For example, a fever may be suppressed because anti-inflammatory therapy is being given. When an infection is being treated, the health professional should be alert to medication reactions, especially to antibiotics.

Pregnancy and Contraception
Spontaneous abortion and premature delivery are more common for women with SLE than for healthy women. To minimize risks to both mother and baby, a pregnant woman with lupus should be closely supervised by an obstetrician familiar with lupus. The safety of oral contraceptives for women with lupus is currently under investigation. The use of an intrauterine device (IUD) is not recommended because of the lupus patient's increased risk of infection.

Surgery
Surgery may exacerbate the symptoms of SLE. Hospitalization may be required for otherwise minor procedures, and postoperative discharge may be delayed. If it is elective, the surgery (including dental surgery and tooth extraction) should be postponed until lupus activity subsides.

Immunizations
Immunizations with killed vaccines have not been shown to exacerbate SLE. However, live vaccines with attenuated organisms are not advisable. A lupus patient should consult her or his doctor before receiving any immunizations, even routine ones.

Medications

SLE management should include as few medications for as short a time as possible. Some patients never require medications, and others take them only as needed or for short intervals, but many require constant therapy with variable doses. Despite their usefulness, no drugs are without risks. Medications frequently used to control the symptoms are nonsteroidal anti-inflammatory drugs (NSAIDs), antimalarials, corticosteroids, and Immunosuppressives. Other medications may be necessary to control specific manifestations. Before prescribing a medication, it is helpful to scrutinize a patient's past response to treatments. A careful drug history should be taken; in particular, hypersensitivities or allergies to certain drugs should be noted, as these may aggravate the lupus. Patient and family education about medications and their side effects is essential.

The goals for prescribing medications for a patient with lupus include

- reducing tissue inflammation caused by the disease,
- suppressing immune system abnormalities that are responsible for tissue inflammation,
- preventing flares and treating them when they do occur, and
- minimizing complication

Lupus patients should work with their doctors to develop their medication treatment plan. Patients should thoroughly understand the reason for taking a drug, its action, dose, administration times, and common side effects. Pharmacists also can be a good resource for patients in helping them understand their medication treatment plan. If a patient experiences a problem believed to be related to a medication, the patient should notify her or his doctor immediately. It can be dangerous to suddenly stop taking some medications, and patients should not stop or change treatments without first talking to their doctor.

The array of drugs and the complexity of treatment plans can be overwhelming and confusing. Newly diagnosed patients and patients whose treatment plans have changed should be closely followed and have immediate access to a nurse or doctor if they are having problems with the prescribed medications. Most SLE patients do well on lupus medications and experience few side effects. Those who do experience negative side effects should not become discouraged, because alternative drugs are often available.

Health professionals should review drug treatment plans with the lupus patient at each office visit to determine her or his understanding of and compliance with the plan. Questions should be encouraged and additional teaching done to reinforce or provide additional information as needed. It is important to note that lupus patients often require drugs for the treatment of conditions commonly seen with the disease. Examples of these types of medications include diuretics, antihypertensives, anticonvulsants, and antibiotics.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

The NSAIDs comprise a large and chemically diverse group of drugs that possess analgesic, anti-inflammatory, and antipyretic properties. Pain and inflammation are common problems in patients with SLE, and NSAIDs are usually the drugs of choice for patients with mild SLE with little or no organ involvement. Patients with serious organ involvement may require more potent anti-inflammatory and immunosuppressive drugs.

Types of NSAIDs

There are as many as 70 NSAIDs on the market, and new ones are constantly becoming available. Some can be purchased as over-the-counter preparations, whereas larger doses of those drugs or other preparations are available only by prescription. For example, prescriptions are required for diclofenac sodium (Voltaren), indomethacin (Indocin), diflunisal (Dolobid), and nabumetone (Relafen).

Mechanism of Action and Use

The therapeutic effects of NSAIDs stem from their ability to inhibit the release of prostaglandins and leukotrienes, which are responsible for producing inflammation and pain. NSAIDs are very useful in treating joint pain and swelling

and muscle pain. They may also be used to treat pleuritic chest pain. An NSAID may be the only drug needed to treat a mild flare; more active disease may require additional medications.

Although all NSAIDs appear to work in the same way, not everyone has the same effect on every person. In addition, patients may do well on one NSAID for a period of time, then, for some unknown reason, derive no benefit from it. Switching the patient to a different NSAID should produce the desired effects. Patients should use only one NSAID at any given time.

Side/Adverse Effects

Gastrointestinal: Dyspepsia, heartburn, epigastric distress, and nausea; less frequently, vomiting, anorexia, abdominal pain, GI bleeding, and mucosal lesions. Misoprostol (Cytotec), a synthetic prostaglandin that inhibits gastric acid secretion, may be given to prevent GI intolerance. It prevents gastric ulcers and their associated GI bleeding in patients receiving NSAIDs.

Genitourinary: Fluid retention, reduction in creatinine clearance, and acute tubular necrosis with renal failure.

Hepatic: Acute reversible hepatotoxicity.

Cardiovascular: Hypertension and moderate to severe noncardiogenic pulmonary edema.

Hematologic: Altered hemostasis through effects on platelet function.

Other: Skin eruption, sensitivity reactions, tinnitus, and hearing loss.

Pregnancy and Lactation: NSAIDs should be avoided during the first trimester and just before delivery; they may be used cautiously at other times during pregnancy. NSAIDs appear in breast milk and should be used cautiously by breastfeeding mothers.

Antimalarials

This group of drugs was first developed during World War II because quinine, the standard treatment for malaria, was in short supply. Investigators discovered antimalarials could also be used to treat the joint pain that occurs with rheumatoid arthritis. Subsequent use of antimalarials showed that they are effective in controlling lupus arthritis, skin rashes, mouth ulcers, fatigue, and fever. They have also been shown to be effective in the treatment of DLE. Antimalarials are not used to manage more serious, systemic forms of SLE that

affect the organs. It may be weeks or months before the patient notices that these drugs are controlling disease symptoms.

Types of Antimalarials
The drugs most often prescribed are hydroxychloroquine sulfate (Plaquenil) and chloroquine (Aralen).

Mechanism of Action and Use
The anti-inflammatory action of these drugs is not well understood. In some patients who take antimalarials, the total daily dose of corticosteroids can be reduced. Antimalarials also affect platelets to reduce the risk of blood clots and lower plasma lipid levels.

Side/Adverse Effects

Central Nervous System: Headache, nervousness, irritability, dizziness, and muscle weakness.

Gastrointestinal: Nausea, vomiting, diarrhea, abdominal cramps, and loss of appetite.

Ophthalmologic: Visual disturbances and retinal changes manifested by blurring of vision and difficulty in focusing. A very serious potential side effect of antimalarial drugs is damage to the retina. Because of the relatively low doses used to treat SLE, the risk of retinal damage is small. However, patients should have a thorough eye examination before starting this treatment and every 6 months thereafter.

Dermatologic: Dryness, pruritus, alopecia, skin and mucosal pigmentation, skin eruptions, and exfoliative dermatitis.

Hematologic: Blood dyscrasia and hemolysis in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency.

Pregnancy
Antimalarials are considered to have a small risk of harming a fetus and should be discontinued in lupus patients who are attempting to become pregnant.

Corticosteroids

Corticosteroids are hormones secreted by the cortex of the adrenal gland. SLE patients with symptoms that do not improve or who are not expected to respond to NSAIDs or antimalarials may be given a corticosteroid. Although corticosteroids have potentially serious side effects, they are highly effective in reducing inflammation, relieving muscle and joint pain and fatigue, and

suppressing the immune system. They are also useful in controlling major organ involvement associated with SLE. These drugs are given in much higher doses than the body produces and act as potent therapeutic agents. The decision to use corticosteroids is highly individualized and is dependent upon the patient's condition.

Once the symptoms of lupus have responded to treatment, the dose is usually tapered until the lowest possible dose that controls disease activity is achieved. Patients must be monitored carefully during this time for flares or recurrence of joint and muscle pain, fever, and fatigue that can result when the dosage is lowered. Some patients may require corticosteroids only during active stages of the disease; those with severe disease or more serious organ involvement may need long-term treatment.

Treatment with corticosteroids must not be stopped suddenly if they have been taken for more than 4 weeks. Administration of corticosteroids causes the body's own production of adrenal hormones to slow down or stop, and adrenal insufficiency will result if the drug is stopped suddenly. Tapering the dose allows the body's adrenal glands to recover and resume production of the natural hormones. The longer a patient has been on corticosteroids, the more difficult it is to lower the dose or discontinue use of the drug.

Types of Corticosteroids
Prednisone (Orason, Meticorten, Deltasone, Cortan, Sterapred), a synthetic corticosteriod, is most often used to treat lupus. Others include hydrocortisone (Cortef, Hydrocortone), methlyprednisolone (Medrol), and dexamethasone (Decadron). Corticosteroids are available as a topical cream or ointment for skin rashes, as tablets, and as an injectable for intramuscular or intravenous administration.

Mechanism of Action and Use
The frequently prescribed corticosteroids are highly effective in reducing inflammation and suppressing the immune response. These drugs may be used to control exacerbation of symptoms and are used to control severe forms of the disease. The drug is usually administered orally. During periods of serious illness, it may be administered intravenously; once the patient has been stabilized, oral administration should be resumed.

Side/Adverse Effects

Central Nervous System: Convulsions, headache, vertigo, mood swings, and psychosis.

Cardiovascular: Congestive heart failure (CHF) and hypertension.

Endocrine: Cushing's syndrome, menstrual irregularities, and hyperglycemia.

Gastrointestinal: GI irritation, peptic ulcer, and weight gain.

Dermatologic: Thin skin, petechiae, ecchymoses, facial erythema, poor wound healing, hirsutism, and urticaria.

Musculoskeletal: Muscle weakness, loss of muscle mass, and osteoporosis.

Ophthalmologic: Increased intraocular pressure, glaucoma, exophthalmos, and cataracts.

Other: Immunosuppression and increased susceptibility to infection.

Pregnancy and Lactation
Corticosteroids cross the placenta, but can be used cautiously during pregnancy. They also appear in breast milk; patients taking large doses should not breastfeed.

Immunosuppressives

Immunosuppressive agents are generally used to reduce rejection of transplanted organs. They are also used in serious, systemic cases of lupus in which major organs such as the kidneys are affected or in which there is severe muscle inflammation or intractable arthritis. Because of their steroid-sparing effect, immunosuppressives may also be used to reduce or sometimes eliminate the need for corticosteroids, thereby sparing the patient from undesirable side effects of corticosteroid therapy.

Immunosuppressives can have serious side effects. Patients need to understand, however, that side effects are dose dependent and are generally reversible by reducing the dose or stopping the medication.

Types of Immunosuppressives
A variety of immunosuppressive drugs is available to treat lupus. Although they have different mechanisms of action, each type functions to decrease or prevent an immune response. The immunosuppressives most frequently used with SLE patients are azathioprine (Imuran), cyclophosphamide (Cytoxan), methotrexate (Rheumatrex), and cyclosporine (Sundimmune, Neoral).

Mechanism of Action and Use
Drugs like azathioprine, methotrexate, and cyclosporine are referred to as antimetabolite agents. These drugs block metabolic steps within immune cells and then interfere with immune function. Cytotoxic drugs like cyclophosphamide

work by targeting and damaging autoantibody-producing cells, thereby suppressing the hyperactive immune response and reducing disease activity.

Side/Adverse Effects
There are many serious risks associated with the use of immunosuppressives. They include immunosuppression (resulting in increased susceptibility to infection), bone marrow suppression (resulting in decreased numbers of RBCs, WBCs, and platelets), and development of malignancies.

Dermatologic: Alopecia (cyclophosphamide only).

Gastrointestinal: Nausea, vomiting, stomatitis, esophagitis, and hepatotoxicity.

Genitourinary: Hemorrhagic cystitis, hematuria, amenorrhea, impotence, and gonadal suppression (cyclophosphamide only).

Hematologic: Thrombocytopenia, leukopenia, pancytopenia, anemia, and myelo-suppression.

Respiratory: Pulmonary fibrosis.

Other: Increased risk of serious infections or malignancies.

Pregnancy and Lactation: Use of immunosuppressives presents definite risks to the fetus. Female patients should use contraceptive measures during treatment and for 12 weeks after ending azathioprine therapy. Azathioprine may pass into breast milk, and women using this drug should consult with their doctors before breastfeeding.

Health Maintenance and Preventative Care

Despite the symptoms of lupus and the potential side-effects of treatment, people with lupus can maintain a high quality of life overall. One key to managing lupus is to understand the disease and its impact. Learning to recognize the warning signs of a flare can help the patient take steps to ward it off or reduce its intensity. Many people with lupus experience increased fatigue, pain, a rash, fever, abdominal discomfort, headache, or dizziness just before a flare. Developing strategies to prevent flares can also be helpful, such as learning to recognize your warning signals and maintaining good communication with your doctor.

It is also important for people with lupus to receive regular health care, instead of seeking help only when symptoms worsen. Results from a medical exam and laboratory work on a regular basis allows the doctor to note any changes and to

identify and treat flares early. The treatment plan, which is tailored to the individual's specific needs and circumstances, can be adjusted accordingly. If new symptoms are identified early, treatments may be more effective. Other concerns also can be addressed at regular checkups. The doctor can provide guidance about such issues as the use of sunscreens, stress reduction, and the importance of structured exercise and rest, as well as birth control and family planning. Because people with lupus can be more susceptible to infections, the doctor may recommend yearly influenza vaccinations or pneumococcal vaccinations for some patients.

Women with lupus should receive regular preventive health care, such as gynecological and breast examinations. Men with lupus should have the prostate-specific antigen (PSA) test. Both men and women need to have their blood pressure and cholesterol checked on a regular basis. If a person is taking corticosteroids or antimalarial medications, an eye exam should be done at least yearly to screen for and treat eye problems.

Staying healthy requires extra effort and care for people with lupus, so it becomes especially important to develop strategies for maintaining wellness. Wellness involves close attention to the body, mind, and spirit. One of the primary goals of wellness for people with lupus is coping with the stress of having a chronic disorder. Effective stress management varies from person to person. Some approaches that may help include exercise, relaxation techniques such as meditation, and setting priorities for spending time and energy.

Developing and maintaining a good support system is also important. A support system may include family, friends, medical professionals, community organizations, and support groups. Participating in a support group can provide emotional help, boost self-esteem and morale, and help develop or improve coping skills.

Learning more about lupus may also help. Studies have shown that patients who are well-informed and participate actively in their own care experience less pain, make fewer visits to the doctor, build self-confidence, and remain more active.

Alternative and Complementary Therapies

Because of the nature and cost of the medications used to treat lupus and the potential for serious side effects, many patients seek other ways of treating the disease. Some alternative approaches people have tried include special diets, nutritional supplements, fish oils, ointments and creams, chiropractic treatment, and homeopathy. Although these methods may not be harmful in and of themselves, and may be associated with symptomatic or psychosocial benefit, no research to date shows that they affect the disease process or prevent organ damage. Some alternative or complementary approaches may help the patient

cope or reduce some of the stress associated with living with a chronic illness. If the doctor feels the approach has value and will not be harmful, it can be incorporated into the patient's treatment plan. However, it is important not to neglect regular health care or treatment of serious symptoms. An open dialogue between the patient and physician about the relative values of complementary and alternative therapies allows the patient to make an informed choice about treatment options.

Psychosocial Aspects

For the lupus patient, the emotional aspects of dealing with a chronic disease can be overwhelming. They can also make a patient feel isolated from friends, family, and coworkers. Grief, depression, and anger are common reactions of patients about their lupus.

Lupus patients and their families deal with the disease in strikingly different ways. Managing the ups and downs of the disease may put strains on relationships and marriages. Younger patients may fail to assert their independence or develop a life away from home if they feel they cannot cope with their disease on their own. Family members are often confused and frightened over the changes they see and need guidance and constructive suggestions on helping the patient. Children of lupus patients, particularly those too young to really understand the disease, may need special help in coping with their parent’s illness. It is in these areas that the patient, family, and support systems need to be assessed, encouraged, and guided so that they work together as a team. Allowing the patient and her or his family time and freedom to move through different emotional phases without criticism and unrealistic expectations will facilitate acceptance of the disease. Therapists can have a major role in helping a patient adjust and can help with referrals to a social worker, counselor, or community resource, if needed.

Seeking a Diagnosis

It may take some time for a patient to be definitively diagnosed with lupus. During this time, patients may be confused or frustrated by the seeming inability of the doctors they visit to confirm the diagnosis. They may ask, “Why don’t the doctors know?” Part of the difficulty, both for the patient and the doctor, rests in the fact that the diagnosis may seem to be hiding in a forest of confusing, vague, or changeable symptoms.

Before a diagnosis is made, many of a patient’s primary needs are emotional. A lupus patient will, in all likelihood, be on intimate terms with her or his symptoms long before their cause is known. Realistically, she or he is the best authority on these symptoms. A patient may feel frustrated if, after describing symptoms, others do not respect her or his knowledge or do not share the conviction that something is wrong. If the doctor, family, or friends are unsupportive, the

patient's fear, anger, and sense of isolation will only increase. These feelings add stress, which in turn can exacerbate the disease.

Health professionals can help ease these feelings by showing empathy during this difficult time and by reassuring the patient that the symptoms are real and merit serious attention. In addition, treating the patient as a whole person, and not just as a subject with a disease, can be immensely valuable in establishing a trusting relationship with the patient. Such a relationship will help the patient speak freely about symptoms or concerns that she or he may have been unwilling to discuss previously.

After the Diagnosis

Patients will certainly experience a sense of relief once their condition is finally given a name and a tangible identity. At the same time, other emotions — anger, fear, depression, confusion, grief — may also surface.
After the diagnosis, some patients will have an insatiable desire for information about the disease; others may need to work through intense emotions before they can come to grips with their illness and begin to cope productively. The rapport that the health professional has established with the patient can now be used to provide the patient with information, resources, and an accepting atmosphere in which to adjust emotionally. This rapport can set a foundation of hope.

Family Issues

One of the most important emotional issues that lupus patients grapple with is the ongoing and changeable reactions of those closest to them: parents, a spouse, or children. Understanding family dynamics can help the health professional work with the patient to develop positive coping strategies.

Parents
Parents of a lupus patient may react by smothering or — the other extreme — by not taking the disease seriously. Because lupus may be genetic, some parents may feel guilty for having "given" their child the disease.

Spouse or Partner
A spouse or partner often experiences many of the same strong emotions the lupus patient does. Grief, fear, and anger are common emotions for spouses or partners as they deal with the patient's changing physical condition. Well-established roles and responsibilities within the family may change, leading to confusion or conflict. These changes and feelings can affect the daily workings of the relationship.

Children

It is difficult for the children of a lupus patient to deal with the large and complex issues raised by having a sick parent. Some of these issues are tangible, whereas others are scary precisely because of their abstract, unknown nature. Because younger children have difficulty articulating their feelings and concerns, these emotions may go unnoticed or may be acted out in negative or disruptive behaviors. Older children with younger siblings may feel resentment as well as concern.

Developing Effective Coping Skills

Many lupus patients go through phases in which they feel that control over their life is slipping from their own hands into those of an unpredictable and unpleasant disease. This sense of powerlessness can occur not only during flares but also during periods of recuperation and remission. It forces the patient to choose between two options. This choice may be made many times during the course of the illness.

The first option is for the patient to submit to the disease and accept lupus and a lifestyle of illness as her or his identity. This choice may appear attractive to a newly diagnosed patient who is exhausted from the long battle of uncertainties related to lupus or to a long-term patient who is exhausted from fighting the disease. However, this option offers a life of self-pity, negativity, and significantly diminished horizons.

The second option is for patients to create a new identity based on reworked, realistic goals and expectations. Inherent in this second option is a sense of greater control, an improved self-image, and a positive and hopeful attitude. This option requires imagination, resilience, and determination and depends heavily on the existence of an adequate support network that can reinforce gains and buffer the occasional disappointment. This option offers true quality of life.

Perhaps the greatest gift that the health professional can offer patients is the opportunity to choose this second option.

Control Over Feelings and Emotions

Patients must first assess their needs and the needs of those around them; evaluate their personal strengths, resources, and weaknesses; and develop effective communication strategies for dealing with family, friends, and the health care team. The health professional can assist the patient or suggest other professionals who can help. Many health professionals — for example, nurses, health educators, psychologists and psychiatrists, social workers, and occupational and physical therapists — are experienced in rheumatology and lupus. These professionals can educate family and friends about the needs and

circumstances of lupus patients. The therapist can also encourage the patient to seek out other supportive mechanisms, such as:

- local support groups,
- educational and self-management programs offered by the Lupus Foundation of America and the Arthritis Foundation, and
- pen pals.

Control Over Their New Physical Limitations

Lupus patients need to accurately assess their pain and fatigue levels and understand how changes in these levels will affect their ability to work, play, and carry out ADL. Rehabilitation professionals can help patients develop an effective self-management program that sets out achievable goals, realistically paces activities, and avoids overcommitments.

Implications for Health Care Providers

How lupus is defined, diagnosed, and treated and the psychosocial issues involved have implications for the way that healthcare professionals work with a patient who has lupus. For example, a newly diagnosed lupus patient needs help in getting current, accurate information about the disease and in defining realistic expectations and goals. The health professional can clarify information with the patient's doctor, make rounds with the doctor, and act as a liaison between the patient and the doctor, if needed. Frequently, many doctors are involved in caring for a lupus patient at one time. This may increase the patient's confusion and leave gaps in information. Emotional support to the patient is essential. Being available for questions, providing reassurance, and encouraging discussion of fears and anxieties are all crucial roles that the therapist can play.

The patient's tolerance for physical activity and need to control what she or he can do should be respected. The patient should be involved in developing a care plan and daily schedule of activities.

Lupus is a challenge to everyone concerned. Therapy professionals have a key role in its management. Accurate documentation, supportive care, emotional support, patient education, and access to community resources will provide the patient and her or his family with the tools they need to cope effectively.

Health professionals continue to search for better ways to care for lupus patients. Answers to what causes the disease and why certain people are more likely to develop it may one day lead to promising new treatments for or even prevention of the disease. In the meantime, researchers continue to look for new treatments and ways to modify existing ones to diminish or eliminate side effects and to improve quality of life for people who have lupus.

Research

Lupus is the focus of intense research as scientists try to determine what causes the disease and how it can best be treated. Some of the questions they are working to answer include: Why are women more likely than men to have the disease? Why are there more cases of lupus in some racial and ethnic groups? What goes wrong in the immune system, and why? How can we correct the way the immune system functions once something goes wrong? What treatment approaches will work best to lessen lupus symptoms? How do we cure lupus?

To help answer these questions, scientists are developing new and better ways to study the disease. They are doing laboratory studies that compare various aspects of the immune systems of people with lupus with those of other people both with and without lupus. They also use mice with disorders resembling lupus to better understand the abnormalities of the immune system that occur in lupus and to identify possible new therapies.

Identifying genes that play a role in the development of lupus is an active area of research. For example, researchers suspect that a genetic defect in a cellular process called apoptosis, or "programmed cell death," exists in people with lupus. Apoptosis is similar to the process that causes leaves to turn color in autumn and fall from trees; it allows the body to eliminate cells that have fulfilled their function and typically need to be replaced. If there is a problem in the apoptosis process, harmful cells may stay around and do damage to the body's own tissues. For example, in a mutant mouse strain that develops a lupus-like illness, one of the genes that controls apoptosis is defective. When it is replaced by a normal gene, the mice no longer develop signs of the disease. Scientists are studying what role genes involved in apoptosis may play in human disease development.

Studying genes for complement, a series of proteins in the blood that play an important part in the immune system, is another active area of lupus research. Complement acts as a backup for antibodies, helping them destroy foreign substances that invade the body. If there is a decrease in complement, the body is less able to fight or destroy foreign substances. If these substances are not removed from the body, the immune system may become overactive and begin to make autoantibodies.

Recent large studies of families with lupus have identified a number of genetic regions that appear to be associated with risk of SLE. Although the specific genes and their function remain unknown, intensive work in mapping the entire human genome offers promise that these genes will be identified in the near future. This should provide knowledge of the complex factors that contribute to lupus susceptibility.

Researchers are also uncovering the impact of genetic, socioeconomic, and cultural factors on the course and outcome of lupus in Hispanics, African Americans, and Caucasians. Preliminary data show that African American and Hispanic lupus patients typically have more kidney damage compared with Caucasians. In addition, researchers found that African American lupus patients have more skin damage compared with Hispanics and Caucasians, and that the death rate from lupus is higher in African Americans and Hispanics compared with Caucasians.

It is thought that autoimmune diseases, such as lupus, occur when a genetically susceptible individual encounters an unknown environmental agent or trigger. In this circumstance, an abnormal immune response can be initiated that leads to the signs and symptoms of lupus. Research has focused on both the genetic susceptibility and the environmental trigger. Although the environmental trigger remains unknown, microbial agents such as Epstein-Barr virus and others have been considered. Researchers also are studying other factors that may affect a person's susceptibility to lupus. For example, because lupus is more common in women than in men, some researchers are investigating the role of hormones and other male-female differences in the development and course of the disease.

Patients with lupus are at risk of developing atherosclerotic vascular disease. The increased risk is due partly to having lupus and partly to steroid therapy. Preventing atherosclerotic vascular disease in lupus patients is a new area of study. Researchers are studying the most effective ways to manage cardiovascular risk factors and prevent cardiovascular disease in adult lupus patients.

In childhood lupus, researchers are evaluating the safety and effectiveness of statin drugs that lower LDL cholesterol levels as a method of preventing fat buildup in the blood vessels.

One out of five lupus patients experiences symptoms such as headaches, dizziness, memory disturbances, stroke, or changes in behavior that result from changes in the brain or other parts of the central nervous system. Such lupus patients have what is called "neuropsychiatric" lupus. Scientists are applying new tools such as brain imaging techniques to discover cellular activity and specific genes that may cause neuropsychiatric lupus. By uncovering the mechanisms responsible for central nervous system damage in lupus patients, researchers hope to move closer to improved diagnosis and treatment for patients with neuropsychiatric lupus.

Researchers are focusing on finding better treatments for lupus. A primary goal of this research is to develop treatments that can effectively minimize the use of corticosteroids. Scientists are trying to identify combination therapies that may be more effective than single treatment approaches. Another goal is to improve the treatment and management of lupus in the kidneys and central nervous system.

For example, a 20-year study found that combining cyclophosphamide with prednisone helped delay or prevent kidney failure, a serious complication of lupus.

Improving current treatments for lupus patients and improving the reproductive health of women with lupus are also important elements of ongoing lupus research. Specifically, investigators are studying ways to

- minimize the use of immunosuppressives, such as corticosteroids and cyclophosphamide, to decrease unwanted side effects and improve the quality of life for lupus patients;
- develop new therapies with fewer side effects;
- correct underlying immune abnormalities; and
- improve women's reproductive health and evaluate the safety of hormone replacement therapy for women with lupus.

Corticosteroids, such as prednisone, are a mainstay of lupus therapy because they suppress the immune system and reduce inflammation. Unfortunately, they also cause some serious side effects, including osteonecrosis, osteoporosis, and coronary artery disease. Other, less serious side effects can also take a toll on the patient's quality of life. Scientists are investigating how corticosteroid use can be minimized in such a way that their benefits are retained while their side effects are reduced.

Cyclophosphamide also suppresses the immune system and has anti-inflammatory properties. Treatment with cyclophosphamide improves many severe manifestations of lupus. Unfortunately, cyclophosphamide can be toxic. Patients using this drug may experience gastrointestinal complications, alopecia, and an increased risk for infections. In the long term, cyclophosphamide also may damage gonadal tissue and lead to ovarian or testicular failure. Other potential long-term complications include hemorrhagic cystitis, bladder fibrosis, and bladder cancer. At this time, scientists are conducting studies to better understand the long-term effects of cyclophosphamide therapy. In addition, they are exploring the use of additional drugs that might counteract some of the negative side effects of cyclophosphamide, and trying to find the most effective dose regimen that causes the fewest severe side effects.

Scientists are also trying to identify combination therapies that may be more effective than single-treatment approaches. For example, in lupus nephritis patients with moderate kidney scarring, a combination of cyclophosphamide and prednisone is more effective in preserving renal function than is treatment with prednisone alone. In these patients, the combination therapy reduces the likelihood of end-stage renal failure.

While some researchers are examining existing drug and treatment practices, other researchers are developing new treatment regimens. Promising areas of

treatment research include biologic agents, hormones, newer forms of chemotherapy, and nitric oxide.

On the basis of new information about the SLE disease process, scientists are using novel biologic agents to selectively block parts of the immune system. Developing and testing these new drugs, which are based on compounds that occur naturally in the body, is an exciting and promising new area of lupus research. Scientists hope that these naturally occurring substances will cause few side effects. In addition, use of these agents may yield clues to the etiology of the disease.

Preliminary research suggests that white blood cells known as B cells may play a key role in the development of lupus. Biologics that interfere with B cell function or block the interactions of immune cells are active areas of research. These targeted treatments hold promise because they have the advantage of reduced side effects and adverse reactions compared with conventional therapies. Clinical trials are testing the safety and effectiveness of rituximab (also called anti-CD20) in treating people with lupus. Rituximab is a genetically engineered antibody that blocks the production of B cells. Other treatment options currently being explored include reconstructing the immune system by bone marrow transplantation. In the future, gene therapy also may play an important role in lupus treatment.

Because hormones are believed to influence the course and perhaps even the etiology of lupus, many researchers are interested in testing the effects of hormones on lupus patients. For example, animal and human studies have shown benefits associated with dehydroepiandrosterone (DHEA) therapy. DHEA is a naturally occurring hormone present in unusually low concentrations in people with lupus. DHEA is currently being tested in clinical trials to determine if its use can improve the clinical outcome and reduce the prednisone requirements of lupus patients.

Researchers also continue to look for new forms of chemotherapy that work selectively on the immune system. For example, they are testing immunosuppressive drugs, such as cyclosporine and 2 chlorodeoxyadenosine, which strongly suppress immune function. Preliminary clinical studies suggest that these drugs may be used in treating patients with lupus nephritis.

Recent studies have investigated the role of nitric oxide, a natural substance known to promote inflammation. These studies, using mice that develop a lupus-like autoimmune illness, including joint and kidney inflammation, showed that the animals produce abnormally high levels of nitric oxide. When the mice were treated with a drug that blocks nitric oxide formation, development of kidney disease was prevented and joint inflammation was reduced. Additional studies are needed to determine whether nitric oxide plays a role in inflammatory disease

in humans and whether drugs that block the formation or action of nitric oxide will be valuable in treating patients with lupus.

Because of recent improvements in diagnostic tools for lupus and a better understanding of the disease, doctors can now predict the likelihood of a lupus-related miscarriage and identify women at risk for giving birth to babies with neonatal lupus. Doctors and lupus patients can now take measures to prevent miscarriages, and doctors can prepare to treat those babies born with neonatal heart block, the most serious complication of neonatal lupus.
Progress is also being made in another important area of reproductive health. In the past, women with lupus have not been able to use oral contraceptives or take advantage of hormone replacement therapy because of concerns that estrogens exacerbate lupus. However, recent data suggest these drugs may be safe for some women with lupus, and a current study funded by NIAMS, the NIH Office of Research on Women's Health, and the NIH Office of Research on Minority Health is focusing on the safety and effectiveness of oral contraceptives and hormone replacement therapy in women with lupus. This clinical trial is called the Safety of Estrogen in Lupus Erythematosus National Assessment (SELENA). Researchers hope this study will yield options for safe, effective methods of contraception for young women with lupus as well as options for estrogen replacement therapy for postmenopausal women with lupus.

Supplemental Information

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Novel therapeutic agents in clinical development for systemic lupus erythematosus
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Resources

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

NIAMS, a part of the National Institutes of Health (NIH), leads the Federal medical research effort in arthritis and musculoskeletal and skin diseases. NIAMS supports research and research training throughout the United States as well as on the NIH campus in Bethesda, MD, and disseminates health and research information. The National Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse (NAMSIC) is a public service sponsored by NIAMS that provides health information and information sources.

1 AMS Circle
Bethesda, MD 20892–3675
Phone: (301) 495–4484 or (877) 22-NIAMS (226-4267)
TTY: (301) 565–2966

Lupus Foundation of America

The Lupus Foundation of America (LFA) is the main voluntary organization devoted to lupus. LFA assists local chapters in providing services, including education, referrals, and support groups, to people with lupus; works to educate the public about lupus; and supports lupus research. For more information, contact LFA at:

2000 L Street, N.W., Suite 710
Washington, DC 20036
Phone: 202-349-1155
Fax: 202-349-1156
http://www.lupus.org

SLE Foundation

The SLE Foundation supports and encourages medical research to find the cause and cure of lupus, and improve its diagnosis and treatment. It also provides a wide variety of services to help lupus patients and their families. In addition, this voluntary organization conducts a broad-based public education program to raise awareness of lupus, and increase understanding of this serious chronic autoimmune disease. For more information, contact the SLE Foundation at:

149 Madison Ave., Suite 205
New York, NY 10016
Phone: (212) 685–4118
http://www.lupusny.org/

Association of Rheumatology Health Professionals, American College of Rheumatology

The American College of Rheumatology (ACR) is an organization of doctors and associated health professionals who specialize in arthritis and related diseases of the bones, joints, and muscles. The Association of Rheumatology Health Professionals (ARHP), a division of ACR, aims to enhance the knowledge and skills of rheumatology health professionals and to promote their involvement in rheumatology research, education, and quality patient care. The Association also works to advance and promote basic and continuing education in rheumatology for health professionals who provide care to people with rheumatic diseases. For more information, contact ARHP at:

1800 Century Place Suite 250
Atlanta, GA 30345–4300
Phone: (404) 633–3777
http://www.rheumatology.org/

Arthritis Foundation

The Arthritis Foundation is the major voluntary organization devoted to supporting arthritis research and providing educational and other services to individuals with arthritis. It publishes free pamphlets and a magazine for members on all types of arthritis. It also provides up-to-date information on research and treatment, nutrition, alternative therapies, and self-management strategies. Chapters nationwide offer exercise programs, classes, support groups, physician referral services, and free literature. For more information, call your local chapter, listed in the white pages of the phone book, or contact the Arthritis Foundation at:

1330 W. Peachtree Street
Atlanta, GA 30309
Phone: (800) 283–7800
http://www.arthritis.org/

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Lupus

Post-Test

1. Which of the following is the most common form of Lupus? (p. 3)
   A. Systemic Lupus Erythematosus
   B. Discoid Lupus Erythematosus
   C. Drug induced Lupus
   D. Neonatal Lupus

2. Which of the following has been implicated as an activator of drug-induced lupus? (p. 4-5)
   A. Proscar
   B. Crestor
   C. Chlorpromazine
   D. Naproxen

3. Ninety percent of the people who have Lupus are women. (p. 5) A. True B. False

4. _____ is a nearly universal complaint of patients with SLE. (p. 6)
   A. Diarrhea
   B. Headache
   C. Hair loss
   D. Fatigue

5. What is considered the classic sign of SLE? (p. 7)
   A. Clubbed fingers
   B. Dilated pupils
   C. “Butterfly” rash on cheeks and nose
   D. Hepatic tenderness

6. SLE associated joint pain is typically migratory and symmetric. (p. 8) A. True B. False

7. While performing therapeutic exercises, a Lupus patient complains of shortness of breath, chills, and anterior chest pain that is relieved by sitting up. This patient is demonstrating symptoms typically associated with _____. (p. 10)
   A. Pericarditis
   B. Livedo reticularis
   C. Venous thrombosis
   D. SLR nephropathy

8. Cerebrovascular accidents are reported in approximately _____ of patients with Lupus. (p. 13)
   A. 3%
   B. 15%
   C. 22%
   D. 34%

9. Active liver disease is the most common gastrointestinal manifestation seen with SLE. (p. 14)
   A. True B. False

10. SLE affects the immune system, thus reducing the body’s ability to prevent and fight infection. (p. 16) A. True B. False

11. Which of the following genes is NOT associated with Lupus? (p. 19)
    A. HLB-DR1
    B. HLA-DR2
    C. HLA-DR3
    D. C4

12. Lupus is an autoimmune disease. (p. 18) A. True B. False

13. Approximately what percentage of Lupus pregnancies end in miscarriage? (p. 21)
    A. 10-15%
    B. 20-25%
    C. 30-35%
    D. 40-45%

14. The American College of Rheumatology has developed a set of ___ diagnostic criteria for Lupus. (p. 22)
    A. 4
    B. 7
    C. 9
    D. 11

15. Which diagnostic test is frequently false positive in Lupus patients? (p. 24)
    A. Anti-Sm
    B. Anti-nDNA
    C. VDRL
    D. aPTT

16. Strict bed rest is usually required to decrease the tiredness due to lupus. (P. 26)
    A. True B. False

17. Which of the following is NOT a medication typically prescribed to control SLE symptoms? (p. 28)
    A. NSAIDS
    B. Corticosteroids
    C. Immunosuppressives
    D. Opioids

18. Lupus patients taking antimalarial medications may have difficulty performing ADL's secondary to _____. (p. 31)
    A. Dizziness
    B. Muscle weakness
    C. Blurred vision
    D. All of the above

19. Patients who are well-informed and participate actively in their own care experience less pain, make fewer visits to the doctor, build self-confidence, and remain more active. (p. 35)
    A. True B. False

20. Lupus researchers are actively studying the genes responsible for "programmed cell death." This process is also known as _____. (p. 40)
    A. Apoptosis
    B. Cytolysis
    C. Genomortis
    D. Chronotasis

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