CLINICAL PRACTICE

LUPUS ERYTHEMATOSUS: CONSIDERATIONS FOR DENTISTRY

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A B S T R A C T

Lupus erythematosus, or LE, is a connective tissue disease that affects a number of organ systems. Patients with this condition can experience several other serious conditions—bleeding, infection, endocarditis, adrenal insufficiency and mucocutaneous disease—that can affect the provision of dental care. The authors describe considerations for managing dental treatment of patients with LE.

Lupus erythematosus, or LE, is commonly referred to as a collagen vascular, or connective, tissue disease. It is a vast disease affecting a number of organ systems. Affected patients are at increased risk of experiencing bleeding, infection, endocarditis, adrenal insufficiency and mucocutaneous disease,[1-8] all of which can affect the provision of dental care. More than 1.5 million people have been diagnosed with LE in the United States.[4,6,7] Dental care providers need to identify these patients, understand the complications associated with these conditions and their implications for dental therapy, and establish appropriate modifications of outpatient dental care. This article provides an overview of the pathogenesis and medical management of LE, as well as dental considerations for patients with this condition.

PATHOGENESIS

LE is believed to arise partly from aberrant immune behavior; the term "autoimmune" is used to describe the reaction of a person's own antibodies (autoantibodies) developed against his or her own tissue. The autoantibodies in LE could be the actual pathogenic agent of tissue destruction, the resultant consequence of tissue damage or the trace left by a true etiologic agent.[1] These immune complexes set off an array of immunological reactions, resulting in activation of the complement system, which attracts neutrophils and macrophages; this in turn leads to vasculitis, fibrosis and tissue necrosis. Recent developments suggest that LE could involve defects in apoptosis, or programmed cell death, leading to an impairment in the body's ability to eliminate unnecessary, damaged or potentially harmful cells.

Systemic lupus erythematosus, or SLE, is a chronic, multisystemic disease of unknown etiology. It is characterized by the production of autoantibodies and immune complexes leading to protean systemic manifestations. The clinical course of SLE is marked by periods of remission and exacerbation. Ninety percent of those affected are young-to-middle-aged women, although it has been reported in men, children and older people.[4] Genetic, hormonal, racial and environmental factors all contribute to SLE. Specifically, SLE occurs more frequently in patients who have human leukocyte anti-

TABLE 1

PROPORTION OF AUTOANTIBODIES ASSOCIATED WITH LUPUS ERYTHEMATOSUS AND OTHER RHEUMATIC DISEASES.*

AUTOANTIBODY TYPE	PRESENCE IN AUTOIMMUNE DISEASE (PERCENTAGE OF CASES)			
	Systemic Lupus Erythematosus	Rheumatoid Arthritis	Sjögren's Syndrome	Diffuse Scleroderma
ANA†	96-100	30-60	95	80-95
Antinative Deoxyribonucleic Acid	60	0-5	0	0
Rheumatoid Factor	20	72-85	75	25-33
Anti-Sm‡	10-25	0	0	0
Anti-Ro§	15-20	0-5	60-70	0
Anti-La**	5-20	0-2	60-70	0

* Adapted from Hellman.[9]
† ANA: Antinuclear antibodies.
‡ Anti-Sm: Antibody to Smith antigen.
§ Anti-Ro: Antibody to Ro OR SS-A antigen.
** Anti-La: Antibody to La OR SS-B antigen.

gen, or HLA, alloantigens DR2 and DR3.[4] Estimates show that 340,000 women currently have SLE in the United States, with one in 1,000 white and one in 250 black women affected.[5] Today, the 10-year survival rate of these patients is approaching 90 percent, with 20-year survival rates near 70 percent.[6] The ever-increasing survival rates in these patients can be attributed to ongoing medical advances, including improved antibiotic therapy and antihypertensive medication, the increased availability and efficacy of hemodialysis and renal transplantation and the more judicious use of lupus-specific therapies.[7] However, these patients still exhibit a high degree of morbidity and die—at a rate three times that of the general population—of active disease or complications of therapy.[8]

FORMS OF LUPUS ERYTHEMATOSUS

Although this article focuses on the systemic form of lupus, a brief discussion of the various types of LE is warranted. Previously, LE was divided into two major forms: SLE and discoid lupus erythematosus, or DLE. Now, however, the classification of LE has been modified to include SLE; a bullous form of LE; a neonatal form, or NLE; a chronic cutaneous form, or CCLE; and a subacute cutaneous form, or SCLE. There is also a lupuslike syndrome caused by various medications referred to as drug-related lupus. Many different drugs have been implicated in this disease; however, lovastatin, D-penicillamine, L-tryptophan, procainamide, hydralazine and isoniazid cause the disorder with appreciable frequency, although very few people develop clinical manifestations.[2]

CCLE and SCLE are primarily dermatologic diseases that almost always are restricted to the skin, usually face and scalp, and the oral mucosa. They most commonly affect middle-aged women. These conditions are not life-threatening unless SLE develops, which is rare.The lesions of CCLE and SCLE appear as round, erythematous plaques with hyperpigmented margins on both skin and oral mucosa. Commonly, scars form and skin pigmentation is lost as the lesion expands peripherally. Oral manifestations are most commonly seen on the buccal mucosa, gingiva and vermilion. These lesions can be plaquelike or erosive and are classified as discoid lesions. The medical management of and oral considerations in treating this condition focus primarily on the cutaneous and mucosal manifestations of the disease.[3]

DIAGNOSIS AND LABORATORY EVALUATION

Because of the many nonspecific clinical manifestations of SLE, the presence of antinuclear antibodies, or ANA, in the blood under indirect immunofluorescence is used to confirm a diagnosis. Patients with CCLE and SCLE might not test positive for ANA, while more than 99 percent of patients with SLE will have detectable ANA. However, a positive ANA test is not specific for SLE. Systemic lupus is characterized by the production of numerous autoantibodies—including antinuclear antibodies; antinative deoxyribonucleic acid, or DNA; rheumatoid factor; antibody to Smith antigen; antibody to Ro, or SS-A, antigen; and antibody to La, or SS-B, antigen—many of which produce specific laboratory and clinical abnormalities.[9] However, these autoantibodies, summarized in Table 1, also can be seen in a number of nonlupus conditions such as rheumatoid arthritis.

CLINICAL MANIFESTATIONS

As mentioned previously, the manifestations of SLE are protean (Table 2), with no typical pattern of presentation; small-vessel vasculitis occurs as a result of immune-complex deposition and leads to renal, cardiac, hematologic, mucocutaneous and central nervous system destruction. In addition, polyserositis (inflammation of the serous membranes) results in joint, peritoneal and pleuropericardial symptoms. A set of diagnostic criteria has been established for the classification and the diagnosis of SLE (Box, "Criteria for the Diagnosis of Systemic Lupus Erythematosus").

As mortality rates continue to decline with continued advances in medical technology, health care practitioners' attention will be consumed by issues such as comorbidity, complications of therapy and overall quality of life—including oral health. Currently, 50 percent of all deaths in patients with SLE result from major end-organ system involvement.[10] Apart from skin, the kidney is the organ most commonly affected by SLE; 5 to 22 percent of SLE patients progress to end-stage renal disease, or ESRD, and require hemodialysis or transplantation.[11] The extent of renal damage can range from subclinical to aggressive and irreversible. Localization of immune complexes in the kidney is the precipitating factor in the development of lupus-related nephritis and can lead to a rapidly progressing glomerulonephritis or a less aggressive form of renal disease that results from cumulative, chronic tissue injury during previous flares of SLE. Ultimately, cell proliferation, inflammation, necrosis and fibrosis result in significant impairment of renal function. This translates to creatinine clearance of less than 80 milliliters per minute (normal being 90-130 mL/min.) or serum creatinine greater than 1.5 milligrams per deciliter (normal being 0.6-1.2 mg/dL).[12]

Treatment of active lupus nephritis, as with most of the systemic disease associated with SLE, consists of glucocorticosteroid and/or immunosuppressive therapy. Commonly, patients are maintained at prednisone doses of 1 mg per kilogram per day of body weight for up to eight weeks, then are tapered down to minimize associated glucocorticosteroid morbidity. The use of adjunctive cytotoxic immunosuppressive drugs, such as cyclophosphamide, have been shown to be more efficacious than are steroids alone in preventing acute active nephritis, preventing renal scarring and therefore reducing the risk of end-stage renal failure.[13] When patients progress to ESRD, hemodialysis and ultimately renal transplantation are the treatments of choice.

An often underrecognized aspect of SLE is the significant neuropsychiatric signs and symptoms found in 10 to 20 percent of the patients who have the disease. Diffuse and focal cerebral dysfunction—including psychosis, seizures and cerebrovascular accidents—in addition to peripheral sensorimotor

TABLE 2

PREVALENCE RATES OF DISEASES ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS.*

DISEASE OR CONDITION	PREVALENCE (%)
Renal Disease	
End-stage renal disease	5-22
Neuropsychiatric Disease	
Organic brain syndrome	20
Psychosis	10
Seizures	15
Symmetrical sensorimotor peripheral neuropathy	10
Cerebrovascular accidents	5
Cardiac Disease	
Valvular pathosis	18-74
Atherosclerosis	20
Hematologic Disease	
Anemia	70
Leukopenia	45
Thrombocytopenia	25
Mucocutaneous Disease	
Oral-mucosal lesions	80
Xerostomia	80-100
Periodontal disease	85-95
Photosensitivity	50
Skin lesions/discoid lupus erythematosus	20
Musculoskeletal Disease	
Myalgia	30
Arthritis	90
Temporomandibular joint disorder symptoms	60

* Based on information from Petri[5]; Hellman[9]; Fessler and Boumpas[10]; Boumpas and colleagues[12]; and Rhodus and Johnson.[25]

CRITERIA FOR THE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS.*

Arthritis
Serositis
Mucocutaneous disease (malar rash, discoid rash, photosensitivity, oral ulcers)
Renal disease (proteinuria)
Neurological disease (psychosis, seizures)
Hematologic disease (hemolytic anemia, thrombocytopenia, leukopenia)
Immunological manifestations (lupus erythematosus cell, antinative deoxyribonucleic acid, false-positive Venereal Disease Research Laboratory test results)
Antinuclear antibodies

* Based on information from Peacock and Cooper[4]; Petri[5]; and Gladman.[7] A diagnosis of SLE can be made with reasonable probability if four of the 11 criteria are met. Serology (antinuclear antibodies) is used to confirm a diagnosis.

neuropathies account for more than 60 percent of neuropsychiatric manifestations.[14] Such neurological changes could be the first SLE sign the clinician sees and should be looked at suspiciously when they occur in undiagnosed young patients.

Neuropsychiatric lupus results from two mechanisms: direct immune-mediated injury to the central nervous system and events occurring secondary to complications of therapy or a different major organ disease. Primary neurological events in these patients occur during clinically or serologically active disease and can precede, coincide with or follow a lupus diagnosis.[15] Microvascular injury, mainly multifocal cortical microinfarctions resulting from immunologically mediated vascular occlusion, constitutes the primary abnormality in neuropsychiatric lupus.[12]

The medical management of neuropsychiatric lupus varies according to the extent of disease and the underlying cause. Glucocorticosteroid therapy, including pulse therapy, is often used in severe cases.

Improvements in diagnostic methods have focused increased attention on the cardiac manifestations of SLE. Some studies have shown that cardiac disease accounts for up to one-third of all deaths in patients with SLE.[16,17] Accelerated atherosclerosis and valvular heart disease constitute the primary pathologies in such patients; the two most common acute life-threatening cardiac conditions include myocardial infarction, or MI, and cardiac tamponade. The incidence of MI in these patients is reported to be nine times higher than predicted population-based rates,[18] and it is not uncommon in patients younger than 35 years of age. The etiology of this cardiac disease appears to be multifactorial and includes accelerated atherosclerosis, coronary arteritis, antiphospholipid vasculitis and in situ thrombosis. Also, up to 53 percent of all SLE patients have three or more cardiac risk factors, including obesity, hypercholesterolemia and hypertension.[16]

Valvular heart disease in patients with SLE has been well-documented in the medical and dental literature.[17,19,20] The most common of all cardiac lesions in these patients, originally described by Libman and Sacks,[21] involves the endocardium. However, lupus-related valvular pathoses can include valve leaflet thickening with or without dysfunction (in other words, regurgitation or stenosis), in addition to the nonbacterial verrucous endocarditis lesions known as Libman-Sacks endocarditis.[19] The prevalence of cardiac valvular involvement in SLE patients has been estimated to range from 18 to 74 percent depending on the cohort of patients studied and the means of examination used.[19,22] The non–Libman-Sacks valvular changes can be identified by echocardiography and can progress to hemodynamically significant lesions that require surgical valve replacement.[23]

Glucocorticosteroids are the mainstay of therapy in managing the cardiac pathology of this disease, even though they can facilitate valvular damage, while routine cardiac medications are used for the management of secondary cardiac conditions.

Hematologic disease—primarily anemia, leukopenia and thrombocytopenia—is a significant aspect of SLE or its treatment. Thrombocytopenia occurs in up to 25 percent of patients, with extreme thrombocytopenia (less than 20,000 platelets per mL) occurring in 5 to 10 percent of patients.[12] The pathogenesis of thrombocytopenia results from increased phagocytosis of autoantibody-coated platelets by spleen, liver, bone marrow and lymph node macrophages. These patients are at a higher risk of bleeding, either spontaneously or after trauma such as that incurred in periodontal and oral surgical procedures. Substantial hemorrhagic tendencies in a patient can indicate an aggressive form of SLE and can be seen in an acute flare.

Medical management of thrombocytopenia in these pa-

TABLE 3

PROTOCOL FOR THE MANAGEMENT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS RECEIVING GLUCOCORTICOID THERAPY.*

DENTAL PROCEDURE	PROTOCOL ACCORDING TO STEROID USE STATUS			
	Previous Systemic Steroid Use	**Current Systemic Steroid Use**	**Daily Alternating Systemic Steroid Use**	**Current Topical Steroid Use**
Routine Dental Procedures	If prior usage lasted for more than two weeks and ceased less than 14-30 days ago: give previous maintenance dose If prior usage ceased more than 14-30 days ago: no supplementation needed Monitor blood pressure during procedure	No supplementation needed Use good local anesthesia Use good postoperative analgesia Monitor blood pressure during procedure	Treat on steroid dosage day; no further supplementation needed	No supplementation needed
Extractions, Surgery or Extensive Dental Procedures	If prior usage lasted for more than two weeks and ceased less than 14-30 days ago: give previous maintenance dose If prior usage ceased more than 14-30 days ago: no supplementation needed Monitor blood pressure during procedure	Double daily dose on day of procedure Double daily dose on first postoperative day when pain is anticipated Use good local anesthesia Use good postoperative analgesia Monitor blood pressure during procedure	Treat on steroid dosage day; give double daily dose on day of procedure Give normal daily dose on first postoperative day when pain is anticipated	No supplementation needed

* Based on information from Glick[34] and Little and colleagues.[35]

tients ranges from platelet transfusions, intravenous administration of γ-globulin or oral administration of danazol and glucocorticosteroids to splenectomy; however, corticosteroid use remains the first line of therapy.[12] Anemia in these patients is most commonly associated with hemodialysis therapy, while leukopenia results from the immunosuppressive therapies.

Patients with SLE might have, in addition to all the other autoantibodies, antiphospholipid antibodies—lupus anticoagulant and anticardiolipin antibodies. When present, these autoantibodies are most commonly identified by a prolonged partial thromboplastin time, or PTT, and make patients susceptible to thrombosis, fetal loss and severe thrombocytopenia.[24]

Mucocutaneous and joint disease also are significant factors in the spectrum of SLE; skin lesions in these patients were among the earliest recognized characteristics and led to the naming of the disease. The cutaneous manifestations of SLE include photosensitive rashes, alopecia (hair loss), periungual telangiectasias (involving the nail folds), and livedo reticularis (purplish-networking discoloration of skin). The malar or butterfly rash, which affects fewer than half of patients with SLE, and the discoid rash are the two most characteristic rashes of SLE. These rashes are commonly photosensitive (exacerbated by exposure to sunlight), superficial

and nonscarring. Cutaneous involvement in patients with SLE does not necessarily correlate with increased systemic disease. However, rash development could indicate a lupus flare.

The mouth is also affected by SLE. More than 75 percent of all SLE patients have oral complaints such as xerostomia, burning mouth and oral ulcerations.[25] Oral lesions in SLE—consisting of ulceration, erythema and/or keratosis—are varied and frequently confused with lichen planus. Commonly, the vermilion, gingiva, buccal mucosa and palate are involved. Also, patients with SLE have significant xerostomia secondary to associated Sjögren's syndrome.[26]

Cutaneous manifestations in 50 to 80 percent of all SLE patients respond to antimalarial therapy, although no controlled studies have been done. In resistant cases, medications such as dapsone, azathioprine, thalidomide, intralesional interferon and retinoids have been used with success. Intraoral lesions often respond to systemic therapies that patients undergo for their medical management. However, intralesional and/or high-potency topical corticosteroids can be used in recalcitrant cases.

Arthritis and Jaccoud arthropathies are the primary conditions of musculoskeletal disease in SLE. Arthralgia with morning stiffness is the most common initial manifestation of SLE, and more than 75 percent of SLE patients develop a true arthritis. This arthritis is often symmetrical and nonerosive and usually involves the hands, wrists and knees.[27] Involvement of the temporomandibular joint, or TMJ, has been documented in up to 60 percent of SLE patients.[28] SLE-related arthritis often is misdiagnosed or can accompany rheumatoid arthritis, or RA. This confusion with RA is furthered by the development of hand deformities in 10 percent of SLE patients. These nonerosive, joint-deforming changes are known as Jaccoud arthropathies because of their similarity to the musculoskeletal changes that occur as a result of rheumatic fever. These deformities result from ligamentous laxity and progress in status from reducible to fixed with increased muscle contractures and atrophy[29] and can affect the TMJ.

DENTAL MANAGEMENT CONSIDERATIONS

The dental considerations in treating patients with LE are directly related to the extraordinary systemic complexities of this autoimmune disease and the sequelae of treatment. Primarily, dental practitioners must be aware of consequences of renal disease and altered drug excretion, immunosuppressive therapy and potential adrenal insufficiency, increased risk of cardiac disease (endocarditis and MI), hematologic abnormalities, mucocutaneous disease and musculoskeletal disorders (including TMJ disorders, or TMDs).

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Renal disease. As renal disease in lupus can range from an asymptomatic state to frank renal failure, the dentist should perform no dental care before assessing the patient's baseline renal function (creatinine clearance, serum creatinine and blood urea nitrogen) and consulting with the patient's physician. Often, patients with advanced disease receive hemodialysis therapy to remove toxic byproducts of metabolism from the blood. Such patients have significant medical problems that can affect the provision of oral health care; these include risk of infection, endocarditis, endarteritis, anemia and risk of increased bleeding. It is preferable for patients receiving hemodialysis therapy to undergo dental treatment on nondialysis days.[30]

Renal impairment and hemodialysis also lead to altered drug metabolism, distribution and elimination.[31] Therefore, the dentist needs to use caution and use appropriate dosing intervals when prescribing medications. In addition, many medications—including penicillin, sulfonamides and nonsteroidal anti-inflammatory agents, or NSAIDs—have been implicated as causative agents in acute lupus flares and should be used judiciously.[32]

Immunosuppressive therapy. Most end-organ lupus disease is managed with glucocorticosteroids and/or cytotoxic medications. These medications can alter the provision of dental care by actions such as adrenocortical suppression in patients taking long-term glucocorticosteroids and an altered immune response in patients taking cyclophosphamide and related cy-

SUMMARY: MANAGEMENT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS.

BEFORE DENTAL CARE

- Consult with the patient's physician or rheumatologist to assess extent of SLE-related end-organ disease and current therapy (as secondary conditions—such as end-stage renal disease or myocardial infarction—can themselves affect provision of care)
- Conduct complete blood count and prothrombin time/partial thromboplastin time tests before performing extensive surgical procedures to assess risk of infection and bleeding
- Consider performing a routine chemistry panel in patients with lupus nephritis
- Postpone elective care during acute lupus flares or pulse therapy
- Assess potential for adrenal suppression and use replacement therapy when appropriate
- Use antimicrobial premedication to prevent endocarditis when indicated
- Consider using preoperative antibiotics for patients receiving immunosuppressive therapy
- Use stress-reducing measures when appropriate:
  —sedative premedication
  —short morning appointments

DURING DENTAL CARE

- Assess oral-mucosal disease and temporomandibular joint, or TMJ, involvement and treat as appropriate
- Use primary closure and adjunctive hemostatic aids as standard of care
- Use stress-reducing measures when appropriate:
  —use of nitrous oxide (if there is no respiratory disease)
  —use of profound local anesthesia

AFTER DENTAL CARE

- Use appropriate dosing intervals of medications for patients who have renal insufficiency or are receiving hemodialysis
- Use caution when prescribing nonsteroidal antiinflammatory agents or acetylsalicylic acid
- Use caution when prescribing respiratory-depressant drugs for analgesia
- Consider postoperative antibiotic use for patients receiving immunosuppressive therapy
- Consider ordering serial radiographic studies yearly to evaluate TMJ arthropathy

totoxic drugs.

Chronic systemic glucocorticosteroid therapy has a multitude of adverse effects, some of which are osteoporosis, diabetes, renal disease, peptic ulcer disease, liver disease, hypertension and seizures. The dental practitioner should ascertain the patient's current dosage of steroid, as well as the recent dose history, even though it has been suggested that hypothalamic-pituitary-adrenal axis function in patients receiving exogenous glucocorticosteroids cannot be assessed accurately on the sole basis of duration of use and dose.[33] Glucocorticosteroid therapy can cause adrenal suppression for up to one year. However, the patient's stress response usually returns within 14 to 30 days, allowing him or her to deal with the stressful situations that can arise in a dental chair.[34] Accordingly, a number of guidelines for patients who are currently or were previously taking glucocorticoids have been established; they are summarized in Table 3.[34,35]

In addition to providing stress dose supplementation when appropriate, the dentist should use stress-reducing measures, including scheduling short morning appointments, using long-acting local anesthetic, using postoperative analgesia when indicated and considering the use of sedative premedication for apprehensive patients.[34] Dental practitioners should monitor the patient's vital signs at the start of each appointment, consider antimicrobial premedication before performing invasive procedures and place the patient on a schedule of routine recall visits.

Immunosuppressive agents, such as cyclophosphamide—an alkylating agent commonly used in addition to prednisone for the treatment of SLE—work to kill and/or interfere with the proliferative response of lymphocytes. Intravenous intermittent pulse therapy has the most favorable therapeutic index, but treatments are complicated, inconvenient, costly and potentially toxic. Its many adverse effects include myelosuppression, dermatotoxicity, hemorrhagic cystitis, gastroenterotoxicity and hepatotoxicity.[36]

Of concern to dentists is the increased risk of infection and bleeding when treating patients on corticosteroid and cytotoxic therapy. In such cases, the dentist should order a complete blood count, or CBC, with differential before performing invasive procedures; antimicrobial prophylaxis in patients with neutropenia (less than 500 to 1,000 cells per cubic millimeter); and adjunctive hemostatic aids in patients with thrombocytopenia (less than 50,000 cells/mm^3) when appropriate. Side effects of intermittent pulse cyclophosphamide thera-

py occur shortly after treatment and can last for days or weeks.[36] Thus, it would be prudent to schedule elective dental procedures two weeks after monthly pulse therapy.

Cardiac disease. Valvular disease is the most prevalent and clinically significant form of cardiac involvement in patients with SLE.[17,19] According to Luce and colleagues,[20] the prevalence of bacterial endocarditis among patients who have SLE is comparable with that among patients who have prosthetic heart valves and is three times that among patients with rheumatic heart disease.[17] Libman-Sacks endocarditis and thickened valvular leaflet lesions—which possibly are different stages of the same process—can lead to hemodynamic changes and predispose patients to infective endocarditis.[37] Eighteen to 74 percent of patients with SLE have valvular pathology, and up to 3.9 percent of these patients, if treated with glucocorticosteroids, will develop infective endocarditis; this translates to a 1.1 percent overall lifetime risk of infective endocarditis in all patients with SLE.[37,38] These findings correlate with a study by Lehman and colleagues,[39] which demonstrated a 1 percent culture-proven bacterial endocarditis incidence in 571 patients with SLE. Dental practitioners should provide antimicrobial prophylaxis in patients when an echocardiographic valvular pathosis is demonstrated. In patients without demonstrated valvular disease, routine antibiotic prophylaxis is not indicated.[17,19] The American Heart Association regimen should be followed, unless the extent of SLE-related renal damage requires dose modification.[40]

Patients who have had a recent MI (within the last six months) are not candidates for elective dental care. Therefore, procedures should be postponed until at least six months after the MI. The dentist should obtain a thorough list of cardiac medications before beginning treatment, as many of these patients can be taking anticoagulant, antianginal and antihypertensive medications that themselves can affect provision of dental care.[41] Dental practitioners must appreciate a host of medical considerations that affect the dental care of these patients, some of which include the need for sedative premedication, the need for morning appointment scheduling, the use of local homeostatic aids and the risk of acute medical emergency while the patient is in the dental chair.[42,43]

Hematologic abnormalities. Thrombocytopenia is one of the most prevalent hematologic abnormalities affecting patients with SLE.[12] Spontaneous hemorrhage is uncommon unless the platelet count drops below 5,000 per mL or there is an underlying defect of platelet function or other coagulopathy.[44] Patients with lupus anticoagulant will have a prolonged PTT and might be at risk for prolonged bleeding following surgical procedures. The dental practitioner, in coordination with the patient's physician, should consider consultation with a hematologist for patients with a history of impaired hemostasis before performing any extensive dental procedures (including periodontal surgery and surgical extractions). A preoperative CBC can aid the dentist in screening for thrombocytopenia, anemia and leukopenia; a PT/PTT, or prothrombin time/partial thromboplastin time, test and skin bleeding time, or SBT, test can screen for a coagulopathy (such as the presence of lupus anticoagulant). However, prolonged SBT by itself might not always predict clinical bleeding.[45]

Patients might undergo splenectomy as a means of managing their thrombocytopenia; therefore, practitioners treating these patients need to consider special management issues.[46] The use of adjunctive hemostatic measures is recommended with such patients; good surgical technique, primary closure and local hemostatic aids (including microfibrillar collagen and oxidized regenerated cellulose) should be used to reduce potential postoperative bleeding. Also, the perioperative use of topical tranexamic mouthrinses or systemic epsilon-aminocaproic acid have been shown to aid the hemostasis of patients with thrombocytopenia by inhibiting fibrinolysis after clot formation.[47,48]

Judicious invasive emergency dental care can be performed on patients with platelet counts as low as 20,000 per mL. However, elective dental treatment should be postponed until platelet levels reach 50 to 60,000 per mL. Platelet transfusions should be considered only when local measures fail. Local anesthesia in the form of block injections should be avoided when the platelet count is less than 20,000 per mL because of the possibility of hematoma formation and airway obstruction. Instead, the practitioner should use infiltration and intraligamentary injections. The use of platelet-inhibiting salicylates or NSAIDs for postoperative pain management

should be avoided.[48]

With patients who have significant anemias, which often are secondary to hemodialysis treatments, dentists should use caution when prescribing respiratory-depressant narcotics for analgesia. If patients are leukopenic, the dentist should calculate the absolute neutrophil count, or ANC. Antimicrobial premedication should be administered before dental procedures when the patient's ANC is less than 1,000 per mL; invasive elective or emergency care should be postponed until the ANC is more than 500 per mL.[49]

Mucocutaneous disease. Historically, oral ulceration has been the only oral complication of LE reported. However, patients with LE are affected by a variety of orofacial problems, including burning mouth, xerostomia and salivary gland disease, TMDs, periodontal disease, dysgeusia and oral mucosal lesions. Rhodus and Johnson[25] reported a high incidence (81.3 to 87.5 percent) of various oral lesions (including ulcers, angular cheilosis, mucositis and glossitis) and a high incidence (75.0 to 87.5 percent) of subjective oral conditions (including glossodynia, dysgeusia, dysphagia and dry mouth). Recently, other mucosal lesions such as oral hairy leukoplakia, not common to SLE patients, have been reported.[50]

It has been suggested that many of the oral conditions of SLE might directly result from salivary gland dysfunction and might be independent of SLE.[25] However, traditional thought holds that most of the oral lesions of SLE are caused by vasculitis and appear as frank ulceration or mucosal inflammation. Lip lesions commonly have a central atrophic area surrounded by a keratinized white border with small radiating striae. Intraoral lesions differ somewhat because of the thinner mucosal epithelium. They typically appear as a central, eroded, red, atrophic area surrounded by a thin elevated keratotic margin that runs into small white lines. Often, the oral manifestation of lupus could be the initial sign of the disease.

The diagnosis of these lesions is accomplished by the demonstrated presence of immunoglobulin and component C3 in the basement membrane via direct fluorescent antibody staining of biopsy specimens. This lupus band test is an excellent means of differentiating lupus lesions from lichen planus, which is often clinically and histologically indistinguishable from other forms of leukoplakia.[51]

Dentists should be familiar with the oral manifestations and complaints of SLE and offer appropriate modalities of treatment to these patients. Xerostomia can significantly increase the occurrence of dental caries and predispose patients to yeast infections, especially when used along with immunosuppressive agents like prednisone. Management of xerostomia and salivary gland disease can range from palliative measures to improve oral comfort (use of saliva substitutes and elimination of fermentable carbohydrates and alcoholic and caffeinated beverages from diet) to frequent periodontal recalls and the use of topical fluoride therapy in occlusive splints. Oral ulcerations are often transient, occurring with acute lupus flares, and regress without intervention. Recalcitrant lesions can be treated with high doses of topical corticoids or intralesional steroid injections.[52]

Dentists should emphasize to these patients the importance of optimal oral health in minimizing their susceptibility to complicated oral infections and bacteremias that lead to endocarditis and endarteritis. Frequent recall visits and excellent oral hygiene will enhance the probability of the dentist's detecting dental disease in the absence of pain, as pulpal obliteration from long-term corticosteroid use can reduce pain perception.[53]

Musculoskeletal disorders and the TMJ. Connective tissue diseases, like SLE, can result in an intra-articular vasculitis, which alters collagenous tissue. This alteration leads in turn to synovitis, joint adhesions and altered joint mechanics, all of which can affect the TMJ.[28,54] Therefore, patients with SLE-related arthritis of the TMJ might experience pain and/or mechanical dysfunction. In patients with a history of, or risk factors for, SLE-related arthritides, dentists should conduct a thorough examination for TMDs; they also should consider the use of serial panoramic radiographs to document bony changes of the TMJ and the prophylactic use of an intraoral flat-plane occlusal orthotic to unload the joint and minimize intracapsular injury.

CONCLUSION

Lupus erythematosus is a vast and complex disease. Dentists should understand the ramifications of this disease, the results of its treatment and its effect on the provision of dental care (Box, "Summary: Management of Patients With Systemic Lupus Erythematosus"). Before undertaking the dental care of a patient with SLE, a dentist

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must consider the patient's immunosuppressed status, as well as the risks of adrenal insufficiency, hematologic disease, renal insufficiency and endocarditis, and then must diagnose and manage the various oral and dental manifestations of the disease. ■

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