Patient education and prophylactic measures to prevent disease flares are crucial in the care of patients with SLE. Sunscreens (SPF ≥50) and ultraviolet radiation–protective clothing are effective in preventing photosensitivity skin rashes and systemic flares. Low-dose aspirin is frequently prescribed for patients with positive APA assays to prevent thrombotic events. Other treatments for antiphospholipid antibody syndrome (APS) are discussed later. Routine immunizations (e.g., influenza, pneumococcus) with nonlive vaccines are recommended for all patients. Psychological support is essential for patients with SLE because the disease may lead to depression and feelings of being overwhelmed.

Nonsteroidal anti-inflammatory medications may be used for mild arthralgias, but glucocorticoids remain the primary anti-inflammatory agent and one of the most effective medications for SLE. Glucocorticoids are used for almost all manifestations of SLE in regimens ranging from low, alternate-day doses to large, intravenous doses. Given the chronic nature of the disease, glucocorticoids are often used over many years, and the cumulative exposure may lead to extensive toxicity, including obesity, diabetes mellitus, accelerated atherosclerosis, osteoporosis, avascular necrosis, cataracts, and increased risk of infections. To avoid these toxicities, steroid-sparing immunomodulating or immunosuppressant agents are used.

Antimalarial medications (primarily hydroxychloroquine) are effective in SLE and are considered standard care. Antimalarials are especially beneficial for the fatigue, mild arthritis, and mucocutaneous manifestations of SLE. These medications are often used chronically and are safe to use in pregnancy. The most serious side effect is retinal toxicity, although it is uncommon. Patients taking antimalarials should have a baseline and annual ophthalmologic examination with visual field testing.

Azathioprine and methotrexate are immunosuppressive agents prescribed for SLE when glucocorticoids alone are not fully effective or to allow for a reduction in glucocorticoid dose. Toxicities of azathioprine include cytopenias, increased infection risk, and potential malignant hematologic disease. Azathioprine may be used during pregnancy for severe internal organ lupus, especially nephritis. Methotrexate is particularly effective in treating inflammatory arthritis associated with SLE. In addition to cytopenias and infections, liver function abnormalities, alopecia, nausea, and pneumonitis are potential side effects of methotrexate. Because it is teratogenic, methotrexate should be stopped 3 to 6 months before pregnancy. Azathioprine and methotrexate require regular laboratory monitoring.

Mycophenolate mofetil (MMF) is increasingly used to treat patients with internal organ involvement, particularly nephritis. Mycophenolic acid, the active metabolite of MMF, can be used in place of MMF because it may have fewer gastrointestinal side effects for some patients. Clinical trials have shown that MMF is as efficacious as intravenous cyclophosphamide for inducing remission of active lupus nephritis. MMF also has a category D rating in pregnancy, and toxicities include gastrointestinal disturbance and leukopenia.

Patients with neurologic lupus, rapidly progressive nephritis, or vasculitis of internal organs are often treated with cyclophosphamide, the most potent immunosuppressive agent used to treat SLE. Because of potential toxicities, this drug is usually reserved for the most severe manifestations of SLE. Acute toxicities of cyclophosphamide include pancytopenia, alopecia, mucositis, and hemorrhagic cystitis. Long-term use of cyclophosphamide may lead to transitional cell carcinoma, malignant hematologic disease, sterility, premature menopause, and opportunistic infections.

Great potential and optimism exist for biologic immunomodulating agents that focus on various aspects of the immune system, including B cells, interactions between B and T cells, and cytokines. The most promising agents are those that target B cells, which produce autoantibodies. Belimumab, a monoclonal antibody that inhibits B-lymphocyte stimulator, is the first therapeutic agent approved for the treatment of SLE in more than 50 years.

For a deeper discussion of these topics, please see Chapter 35, "Immunosuppressing Drugs including Corticosteroids" in Goldman-Cecil Medicine, *25th Edition.*

SPECIAL ISSUES IN THE CARE OF PATIENTS WITH SLE

Pregnancy

Pregnant women with SLE have higher rates of pregnancy loss (i.e., miscarriage and stillbirths) and preterm delivery (i.e., premature rupture of membranes, preeclampsia, and intrauterine growth restriction) than their healthy counterparts. Lupus activity preceding conception, especially nephritis, hypertension, and APS, are risk factors for pregnancy complications in SLE. Pregnancy itself may place women with SLE at a greater risk of a flare, particularly if the disease was active before conception.

Neonatal lupus is a rare disorder in which maternal anti-SSA/Ro or SSB/La antibodies, or both, cross the placenta and affect the fetus. Mothers with these autoantibodies have a 2% risk of having a child with congenital heart block. These mothers are screened with fetal heart tones and fetal echocardiography beginning at 16 weeks' gestation. Treatment with a fluorinated corticosteroid (i.e., dexamethasone or betamethasone) may be beneficial, but many children with congenital heart block do not survive (30%) or have morbidities, with more than 60% requiring pacemakers.

More common manifestations of neonatal SLE are rashes, cytopenias, and hepatosplenomegaly, all of which typically resolve in 6 to 8 months after maternal antibodies are removed from the child's circulation. Mothers of children with neonatal SLE do not necessarily have SLE themselves.

With careful prenatal screening and planning, women with SLE can successfully have a healthy child. Prenatal monitoring of anti-SSA/Ro and anti-SSB/La antibodies and APAs and prepregnancy consultation with obstetricians caring for high-risk pregnancies are critical. Ideally, women with SLE should have clinical quiescence for 6 months before considering a planned pregnancy.

Hormone Therapy

Hormones were thought to play a role in the development of SLE because of its female predominance. Rheumatologists have historically been hesitant to prescribe estrogen therapy for fear of