heart failure, arrhythmia, or embolic events. As discussed above, patients with SLE are at increased risk for myocardial infarction, usually due to accelerated atherosclerosis, which probably results from immune attack, chronic inflammation, and/or chronic oxidative damage to arteries.

HEMATOLOGIC MANIFESTATIONS

The most frequent hematologic manifestation of SLE is anemia, usually normochromic normocytic, reflecting chronic illness. Hemolysis can be rapid in onset and severe, requiring high-dose glucocorticoid therapy, which is effective in most patients. Leukopenia is also common and almost always consists of lymphopenia, not granulocytopenia; lymphopenia rarely predisposes to infections and by itself usually does not require therapy. Thrombocytopenia may be a recurring problem. If platelet counts are >40,000/μL and abnormal bleeding is absent, therapy may not be required. High-dose glucocorticoid therapy (e.g., 1 mg/kg per day of prednisone or equivalent) is usually effective for the first few episodes of severe thrombocytopenia. Recurring or prolonged hemolytic anemia or thrombocytopenia, or disease requiring an unacceptably high dose of daily glucocorticoids, should be treated with an additional strategy (see "Management of Systemic Lupus Erythematosus" below).

GASTROINTESTINAL MANIFESTATIONS

Nausea, sometimes with vomiting, and diarrhea can be manifestations of an SLE flare, as can diffuse abdominal pain probably caused by autoimmune peritonitis and/or intestinal vasculitis. Increases in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are common when SLE is active. These manifestations usually improve promptly during systemic glucocorticoid therapy. Vasculitis involving the intestine may be life-threatening; perforations, ischemia, bleeding, and sepsis are frequent complications. Aggressive immunosuppressive therapy with high-dose glucocorticoids is recommended for short-term control; evidence of recurrence is an indication for additional therapies.

OCULAR MANIFESTATIONS

Sicca syndrome (Sjögren's syndrome; Chap. 383) and nonspecific conjunctivitis are common in SLE and rarely threaten vision. In contrast, retinal vasculitis and optic neuritis are serious manifestations: blindness can develop over days to weeks. Aggressive immunosuppression is recommended, although there are no controlled trials to prove effectiveness. Complications of systemic and intraorbital glucocorticoid therapy include cataracts (common) and glaucoma.

LABORATORY TESTS

Laboratory tests serve (1) to establish or rule out the diagnosis; (2) to follow the course of disease, particularly to suggest that a flare is occurring or organ damage is developing; and (3) to identify adverse effects of therapies.

TESTS FOR AUTOANTIBODIES (TABLES 378-1 AND 378-3)

Diagnostically, the most important autoantibodies to detect are ANA because the test is positive in >95% of patients, usually at the onset of symptoms. A few patients develop ANA within 1 year of symptom onset; repeated testing may thus be useful. ANA tests using immunofluorescent methods are more reliable than enzyme-linked immunosorbent assays (ELISAs) and/or bead assays, which have less specificity. ANA-negative lupus exists but is rare in adults and is usually associated with other autoantibodies (anti-Ro or anti-DNA). High-titer IgG antibodies to double-stranded DNA (dsDNA) (but not to single-stranded DNA) are specific for SLE. ELISA and immunofluorescent reactions of sera with the dsDNA in the flagellate *Crithidia luciliae* have ~60% sensitivity for SLE; identification of high-avidity anti-dsDNA in the Farr assay is not as sensitive but may correlate better with risk for nephritis. Titers of anti-dsDNA vary over time. In some patients, increases in quantities of anti-dsDNA herald a flare, particularly of nephritis or vasculitis, especially when associated with declining levels of C3 or C4 complement. Antibodies to Sm are also specific for SLE and assist in diagnosis; anti-Sm antibodies do not usually correlate with disease activity or clinical manifestations. Antiphospholipid antibodies are not specific for SLE, but their presence fulfills one classification criterion, and they identify patients at increased risk for venous or arterial clotting, thrombocytopenia, and fetal loss. There are three widely accepted tests that measure different antibodies (anticardiolipin, anti-β_2-glycoprotein, and the lupus anticoagulant). ELISA is used for anticardiolipin and anti-β_2-glycoprotein (both internationally standardized with good reproducibility); a sensitive phospholipid-based activated prothrombin time such as the dilute Russell venom viper test is used to identify the lupus anticoagulant. The higher the titers of IgG anticardiolipin (>40 IU is considered high), and the greater the number of different antiphospholipid antibodies that are detected, the greater is the risk for a clinical episode of clotting. Quantities of antiphospholipid antibodies may vary markedly over time; repeated testing is justified if clinical manifestations of the antiphospholipid syndrome (APS) appear (Chap. 379). To classify a patient as having APS, with or without SLE, by international criteria requires the presence of one or more clotting episodes and/or repeated fetal losses plus at least two positive tests for antiphospholipid antibodies, at least 12 weeks apart; however, many patients with APS do not meet these stringent criteria, which are intended for inclusion of patients into studies.

An additional autoantibody test with predictive value (not used for diagnosis) detects anti-Ro/SS-A, which indicates increased risk for neonatal lupus, sicca syndrome, and SCLE. Women with child-bearing potential and SLE should be screened for antiphospholipid antibodies and anti-Ro, because both antibodies have the potential to cause fetal harm.

STANDARD TESTS FOR DIAGNOSIS

Screening tests for complete blood count, platelet count, and urinalysis may detect abnormalities that contribute to the diagnosis and influence management decisions.

TESTS FOR FOLLOWING DISEASE COURSE

It is useful to follow tests that indicate the status of organ involvement known to be present during SLE flares. These might include urinalysis for hematuria and proteinuria, hemoglobin levels, platelet counts, and serum levels of creatinine or albumin. There is great interest in identification of additional markers of disease activity. Candidates include levels of anti-DNA and anti-C1q antibodies, several components of complement (C3 is most widely available), activated complement products (including those that bind to the C4d receptor on erythrocytes), IFN-inducible gene expression in peripheral blood cells, serum levels of BLyS (B lymphocyte stimulator, also called BAFF), and urinary levels of TNF-like weak inducer of apoptosis (TWEAK), neutrophil gelatinase-associated lipocalin (NGAL), or monocyte chemotactic protein 1 (MCP-1). None is uniformly agreed upon as a reliable indicator of flare or of response to therapeutic interventions. It is likely that a panel of multiple proteins will be developed to predict both impending flare and response to recently instituted therapies. For now, the physician should determine for each patient whether certain laboratory test changes predict flare. If so, altering therapy in response to these changes may be advisable (30 mg of prednisone daily for 2 weeks has been shown to prevent flares in patients with rising anti-DNA plus falling complement). In addition, given the increased prevalence of atherosclerosis in SLE, it is advisable to follow the recommendations of the National Cholesterol Education Program for testing and treatment, including scoring of SLE as an independent risk factor, similar to diabetes mellitus.

MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

There is no cure for SLE, and complete sustained remissions are rare. Therefore, the physician should plan to induce remissions of acute flares and then maintain improvements with strategies that suppress symptoms to an acceptable level and prevent organ damage. Usually patients will endure some adverse effects of medications. Therapeutic choices depend on (1) whether disease manifestations are life-threatening or likely to cause organ damage, justifying aggressive therapies; (2) whether