women are caused by the uricosuric effects of estrogen. Urinary uric acid levels are normally <750 mg per 24 h. Although hyperuricemia (especially levels >535 μmol/L [9 mg/dL]) is associated with an increased incidence of gout and nephrolithiasis, levels may not correlate with the severity of articular disease. Uric acid levels (and the risk of gout) may be increased by inborn errors of metabolism (Lesch-Nyhan syndrome), disease states (renal insufficiency, myeloproliferative disease, psoriasis), or drugs (alcohol, cytotoxic therapy, thiazides). Although nearly all patients with gout will demonstrate hyperuricemia at some time during their illness, up to 50% of patients with an acute gouty attack will have normal serum uric acid levels. Monitoring serum uric acid may be useful in assessing the response to urate-lowering therapy or chemotherapy, with the target goal being a serum urate <6 mg/dL.

Serologic tests for rheumatoid factor (RF), cyclic anticitrullinated peptide (CCP or ACPA) antibodies, ANAs, complement levels, Lyme and antineutrophil cytoplasmic antibodies (ANCA), or antistreptolysin O (ASO) titer should be carried out only when there is clinical evidence to specifically suggest an associated diagnosis, because these have poor predictive value when used for screening, especially when the pretest probability is low. For most of these, there is no value to repeated or serial serologic testing. Although 4–5% of a healthy population will have positive tests for RF and ANAs, only 1% and <0.4% of the population will have RA or SLE, respectively. IgM RF (autoantibodies against the Fc portion of IgG) is found in 80% of patients with RA and may also be seen in low titers in patients with chronic infections (tuberculosis, leprosy, hepatitis); other autoimmune diseases (SLE, Sjögren's syndrome); and chronic pulmonary, hepatic, or renal diseases. When considering RA, both serum RF and anti-CCP antibodies should be obtained as these are complementary. Both are comparably sensitive, but CCP antibodies are more specific than RF. In RA, the presence of anti-CCP and RF antibodies may indicate a greater risk for more severe, erosive polyarthritis. ANAs are found in nearly all patients with SLE and may also be seen in patients with other autoimmune diseases (polymyositis, scleroderma, antiphospholipid syndrome, Sjögren's syndrome), drug-induced lupus (Table 393-2), chronic liver or renal disorders, and advanced age. Positive ANAs are found in 5% of adults and in up to 14% of elderly or chronically ill individuals. The ANA test is very sensitive but poorly specific for lupus, as only 1–2% of all positive results will be caused by lupus alone. The interpretation of a positive ANA test may depend on the magnitude of the titer and the pattern observed by immunofluorescence microscopy (Table 393-4). Diffuse and speckled patterns are least specific, whereas a peripheral, or rim, pattern (related to autoantibodies against double-strand [native] DNA) is highly specific and suggestive of lupus. Centromeric patterns are seen in patients with limited scleroderma (*c*alcinosis, *R*aynaud's phenomenon, *e*sophageal involvement, *s*clerodactyly, *t*elangiectasia [CREST] syndrome) or primary biliary sclerosis, and nucleolar patterns may be seen in patients with diffuse systemic sclerosis or inflammatory myositis.

TABLE 393-4 ANTINUCLEAR ANTIBODY (ANA) PATTERNS AND CLINICAL ASSOCIATIONS

ANA Pattern	Antigen Identified	Clinical Correlate
Diffuse	Deoxyribonucleoprotein	Nonspecific
	Histones	Drug-induced lupus, lupus
Peripheral (rim)	ds-DNA	50% of SLE (specific)
Speckled	U1-RNP	>90% of MCTD
	Sm	30% of SLE (specific)
	Ro (SS-A)	Sjögren's 60%, SCLE, neonatal lupus, ANA(–) lupus
	La (SS-B)	50% of Sjögren's, 15% lupus
	Scl-70	40% of diffuse scleroderma
	PM-1	Polymyositis (PM), dermatomyositis
	Jo-1	PM w/pneumonitis + arthritis
Nucleolar	RNA polymerase I, others	40% of PSS
Centromere	Kinetochore	75% CREST (limited scleroderma)

Abbreviations: ANA, antinuclear antibody; CREST, *c*alcinosis, *R*aynaud phenomenon, *e*sophageal involvement, *s*clerodactyly, and *t*elangiectasia; MCTD, mixed connective tissue disease; PSS, progressive systemic sclerosis; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

Aspiration and analysis of synovial fluid are always indicated in acute monarthritis or when an infectious or crystal-induced arthropathy is suspected. Synovial fluid may distinguish between noninflammatory and inflammatory processes by analysis of the appearance, viscosity, and cell count. Tests for synovial fluid glucose, protein, lactate dehydrogenase, lactic acid, or autoantibodies are not recommended because they have no diagnostic value. Normal synovial fluid is clear or a pale straw color and is viscous, primarily because of the high levels of hyaluronate. Noninflammatory synovial fluid is clear, viscous, and amber-colored, with a WBC count of <2000/μL and a predominance of mononuclear cells. The viscosity of synovial fluid is assessed by expressing fluid from the syringe one drop at a time. Normally, there is a stringing effect, with a long tail behind each synovial drop. Effusions caused by OA or trauma will have normal viscosity. Inflammatory fluid is turbid and yellow, with an increased WBC count (2000–50,000/μL) and a polymorphonuclear leukocyte predominance. Inflammatory fluid has reduced viscosity, diminished hyaluronate, and little or no tail following each drop of synovial fluid. Such effusions are found in RA, gout, and other inflammatory arthritides. Septic fluid is opaque and purulent, with a WBC count usually >50,000/μL, a predominance of polymorphonuclear leukocytes (>75%), and low viscosity. Such effusions are typical of septic arthritis but may also occur with RA or gout. In addition, hemorrhagic synovial fluid may be seen with trauma, hemarthrosis, or neuropathic arthritis. An algorithm for synovial fluid aspiration and analysis is shown in Fig. 393-6. Synovial fluid should be analyzed immediately for appearance, viscosity, and cell count. Monosodium urate crystals (observed in gout) are seen by polarized microscopy and are long, needle-shaped, negatively birefringent, and usually intracellular. In chondrocalcinosis and pseudogout, calcium pyrophosphate dihydrate crystals are usually short, rhomboid-shaped, and positively birefringent. Whenever infection is suspected, synovial fluid should be Gram stained and cultured appropriately. If gonococcal arthritis is suspected, nucleic acid amplification tests should be used to detect either *Chlamydia trachomatis* or *N. gonorrhoeae* infection. Synovial fluid from patients with chronic monarthritis should also be cultured for *M. tuberculosis* and fungi. Last, it should be noted that crystal-induced arthritis and septic arthritis occasionally occur together in the same joint.

DIAGNOSTIC IMAGING IN JOINT DISEASES

Conventional radiography has been a valuable tool in the diagnosis and staging of articular disorders. Plain x-rays are most appropriate and cost effective when there is a history of trauma, suspected chronic infection, progressive disability, or monarticular involvement; when therapeutic alterations are considered; or when a baseline assessment is desired for what appears to be a chronic process. However, in acute inflammatory arthritis, early radiography is rarely helpful in establishing a diagnosis and may only reveal soft tissue swelling or juxtaarticular demineralization. As the disease progresses, calcification (of soft tissues, cartilage, or bone), joint space narrowing, erosions, bony ankylosis, new bone formation (sclerosis, osteophytes, or periostitis), or subchondral cysts may develop and suggest specific clinical entities. Consultation with a radiologist will help define the optimal imaging modality, technique, or positioning and prevent the need for further studies.

Additional imaging techniques may possess greater diagnostic sensitivity and facilitate early diagnosis in a limited number of articular disorders and in selected circumstances and are indicated when conventional radiography is inadequate or nondiagnostic (Table 393-5). *Ultrasonography* is useful in the detection of soft tissue abnormalities, such as tendinitis, tenosynovitis, enthesitis, bursitis, and entrapment neuropathies. Wider use, lower cost, better technology, and enhanced site-specific transducers now allow for routine use in outpatient care. Owing to low cost, portability, and wider use, ultrasound use has grown and is the preferred method for the evaluation of synovial (Baker's) cysts, rotator cuff tears, tendinitis and tendon injury, and