Diagnostic Approach to Polyarticular Joint Pain

ANNA MIES RICHIE, M.D., and MARK L. FRANCIS, M.D.
Southern Illinois University School of Medicine, Springfield, Illinois

Identifying the cause of polyarticular joint pain can be difficult because of the extensive differential diagnosis. A thorough history and a complete physical examination are essential. Six clinical factors are helpful in narrowing the possible causes: disease chronology, inflammation, distribution, extra-articular manifestations, disease course, and patient demographics. Patients with an inflammatory arthritis are more likely to have palpable synovitis and morning stiffness; if the condition is severe, they may have fever, weight loss, and fatigue. Viral infections, crystal-induced arthritis, and serum sickness reactions are common causes of acute, self-limited polyarthritis. Because chronic arthritides may present abruptly, they need to be considered in patients who present with acute polyarticular joint pain. Joint palpation can help to distinguish inflammatory synovitis from the bony hypertrophy and crepitus that typically occur with osteoarthritis. Extra-articular manifestations of rheumatologic disease may be helpful in arriving at a more specific diagnosis. Many classic rheumatologic laboratory tests are nonspecific. A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues. Plain-film radiographs may demonstrate classic findings of specific rheumatologic diseases; however, radiographs can be normal or only show nonspecific changes early in the disease process. **(Am Fam Physician 2003;68:1151-60.**

Members of various family practice departments develop articles for "Problem-Oriented Diagnosis." This is one in a series from the Department of Family and Community Medicine at Southern Illinois University School of Medicine, Springfield. Guest editor of the series is Robert M. Wesley, M.A.

See page 1039 for definitions of strength-of-evidence levels.

Polyarticular joint pain (i.e., pain in more than four joints) poses a diagnostic challenge because of the extensive differential diagnosis[1] *(Table 1)*. Consequently, family physicians need to keep the diagnosis open in evaluating patients who present with pain in multiple joints. For instance, a 50-year-old woman with symmetric, progressive polyarticular joint swelling and prolonged morning stiffness would seem to have rheumatoid arthritis. However, this patient might develop a malar rash and oral ulcers, which would change the diagnosis to systemic lupus erythematosus. Alternatively, the patient might develop thickening of the skin, which would suggest the diagnosis of scleroderma. Thus, a series of visits over time may be necessary to arrive at a specific diagnosis in many patients with polyarticular joint pain. In some patients, it may not be possible to establish a definitive diagnosis.

Because many rheumatologic laboratory tests lack the desired specificity, results should be interpreted in the clinical context and with caution. Tests with low specificity, such as those in arthritis panels, are frequently positive in the general population. Thus, these tests may be misleading.[2] Furthermore, use of tests with low specificity may increase unnecessary testing and attendant costs, result in inappropriate treatment, and have a negative psychologic impact on patients.[3]

In the absence of definitive rheumatologic laboratory tests, the history and physical examination are key to the early diagnosis and treatment of conditions that cause polyarticular joint pain. Indeed, the differential diagnosis can be narrowed through investigation of six clinical factors: disease chronology, inflammation, distribution, extra-articular manifestations, disease course, and patient demographics *(Table 2)*. More common causes of polyarticular joint pain should be considered first.

Disease Chronology

Acute polyarticular joint pain (i.e., pain that has been present for less than six weeks) may be the sign of a self-limited disorder or a harbinger of chronic disease. Although chronic polyarticular arthritides more often develop insidiously, they can present abruptly. Thus, chronic conditions such as rheumatoid arthritis and systemic lupus erythematosus should be considered, at least initially, in patients who present with acute polyarticular joint pain *(Table 3)*.[4-7] To avoid treating a self-limited

TABLE 1
Differential Diagnosis of Polyarticular Joint Pain

Viral infection: human parvovirus (especially B19), enterovirus, adenovirus, Epstein-Barr, coxsackievirus (A9, B2, B3, B4, B6), cytomegalovirus, rubella, mumps, hepatitis B, varicella-zoster virus (human herpes virus 3), human immunodeficiency virus

Indirect bacterial infection (reactive arthritis): *Neisseria gonorrhoeae* (gonorrhea), bacterial endocarditis, Campylobacter species, Chlamydia species, Salmonella species, Shigella species, Yersinia species, *Tropheryma whippelii* (Whipple's disease), group A streptococci (rheumatic fever)

Direct bacterial infection: *N. gonorrhoeae, Staphylococcus aureus,* gram-negative bacilli, bacterial endocarditis

Other infections: *Borrelia burgdorferi* (Lyme disease), *Mycobacterium tuberculosis* (tuberculosis), fungi

Crystal-induced synovitis: gout, pseudogout (calcium pyrophosphate deposition disease), hydroxyapatite

Systemic rheumatic disease: rheumatoid arthritis, systemic lupus erythematosus, polymyositis/dermatomyositis, juvenile rheumatoid arthritis, scleroderma, Sjögren's syndrome, Behçet's syndrome, polymyalgia rheumatica

Systemic vasculitis disease: Schönlein-Henoch purpura, hypersensitivity vasculitis, polyarteritis nodosa, Wegener's granulomatosis, giant cell arteritis

Spondyloarthropathies: ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, reactive arthritis (Reiter's syndrome)

Endocrine disorders: hyperparathyroidism, hyperthyroidism, hypothyroidism

Malignancy: metastatic cancer, multiple myeloma

Others: osteoarthritis, hypermobility syndromes, sarcoidosis, fibromyalgia, osteomalacia, Sweet's syndrome, serum sickness

TABLE 2
Common Causes of Polyarticular Joint Pain

			Distribution				
Disease	*Chronology*	*Inflammation*	*Pattern*	*Symmetry*	*Axial involvement*	*Extra-articular manifestations*	*Female-to-male ratio*
Human parvovirus B19 infection	Acute	Yes	Small joints	Yes	No	Lacy rash, malar rash	3:1 to 4:1
Rheumatoid arthritis	Chronic	Yes	Small and large joints	Yes	Cervical	Subcutaneous nodules, carpal tunnel syndrome	3:1 to 4:1
Systemic lupus erythematosus	Chronic	Yes	Small joints	Yes	No	Malar rash, oral ulcers, serositis (pleuritis or pericarditis)	9:1
Osteoarthritis	Chronic	No	Lower extremity joints, proximal and distal interphalangeal joints, first carpometacarpal joint	Yes/No	Cervical and lumbar	None	1:1 to 2:1
Fibromyalgia	Chronic	No	Diffuse	Yes	Yes	Myalgias, tender points, irritable bowel syndrome	9:1
Ankylosing spondylitis	Chronic	Yes	Large joints	Yes	Yes	Iritis, tendonitis, aortic insufficiency	1:1 to 1:5
Psoriatic arthritis	Chronic	Yes	Large and small joints	Yes/No	Yes/No	Psoriasis, dactylitis ("sausage digits"), tendonitis, onychodystrophy	1:1

TABLE 3

Diagnostic Criteria for Rheumatoid Arthritis, Systemic Lupus Erythematosus, and Fibromyalgia

The rightsholder did not grant rights to reproduce this item in electronic media. For the missing item, see the original print version of this publication.

Palpation of joint capsules can help to distinguish inflammatory synovitis from the noninflammatory bony hypertrophy that often indicates osteoarthritis.

disorder with potentially toxic disease-modifying agents, synovitis should be present for six weeks before rheumatoid arthritis is diagnosed.[4] [Evidence level C, consensus opinion]

Viruses (e.g., human parvovirus B19, hepatitis viruses), crystals, and serum sickness reactions are known causes of acute, self-limited polyarthritis. The specific cause of virus-induced arthritis is not always investigated; thus, the prevalence of viruses as the etiology of arthritis may be underestimated.[8]

Except for *Neisseria gonorrhoeae,* direct bacterial infections in joints seldom cause polyarthritis.[9] Although typically oligoarticular, extra-articular bacterial infections may induce acute arthritis. Classic reactive arthritis, for example, is associated with enteric infections (Salmonella, Shigella, Campylobacter, or Yersinia species) and urogenital infections *(Chlamydia trachomatis)*.

Early gout usually affects only one joint. However, this disease also should be considered in patients with acute polyarticular arthritis, particularly older women who are taking diuretics and have hypertrophy and degenerative changes of the distal interphalangeal (DIP) joints (Heberden's nodes) and proximal interphalangeal (PIP) joints (Bouchard's nodes).[10]

Inflammation

Arthritis is joint pain with inflammation, whereas arthralgia is joint pain without inflammation. The patient who presents with psoriasis and knee pain in the absence of inflammation may have the dual diagnosis of psoriasis and osteoarthritis. However, the patient who also has inflammation probably has psoriatic arthritis, which may require more aggressive therapy. Inflammatory arthritides include infectious arthritis, gout, rheumatoid arthritis, systemic lupus erythematosus, and reactive arthritis.

Cardinal signs of inflammation include erythema, warmth, pain, and swelling. Patients with severe joint inflammation or systemic disease also may present with fatigue, weight loss, or fever.[8] Morning stiffness lasting longer than one hour suggests underlying inflammation.[1] The duration of morning stiffness provides a useful guide to the extent of inflammation. For instance, morning stiffness associated with rheumatoid arthritis may last for hours.[11,12]

Palpation of multiple joint capsules is important to look for soft tissue swelling and effusions that result in edema and influx of inflammatory cells into and around the synovium. Soft tissue swelling should be distinguished from noninflammatory bony hypertrophy, such as Heberden's and Bouchard's nodes, which often indicate osteoarthritis *(Figure 1)*. Crepitus indicates the pres-

FIGURE 1.

The Authors

ANNA MIES RICHIE, M.D., is assistant professor in the Department of Family and Community Medicine at Southern Illinois University School of Medicine, Springfield, where she earned her medical degree and completed a family practice residency and fellowship.

MARK L. FRANCIS, M.D., is associate professor and chief of the Division of Rheumatology at Southern Illinois University School of Medicine. Dr. Francis received his medical degree from Saint Louis University School of Medicine, St. Louis, and completed an internal medicine residency at William Beaumont Army Medical Center, El Paso, where he was chief resident. He also completed three years of a rheumatology fellowship at Walter Reed Army Medical Center, Washington, D.C.

Address correspondence to Anna Mies Richie, M.D., Department of Family and Community Medicine, Southern Illinois University School of Medicine, P.O. Box 19671, Springfield, IL 62794-9671 (e-mail amiesrichie@siumed.edu). Reprints are not available from the authors.

ence of irregularities of the articular cartilage, which most commonly are associated with osteoarthritis, injury, or previous inflammation.

Because findings can be subtle, it is important to palpate each hand joint. Although palpation often can identify synovitis, it may not detect inflammation of more proximal joints in, for example, elderly patients with polymyalgia rheumatica.[13]

Morning stiffness and a history of swelling suggest an inflammatory process but also are characteristic of fibromyalgia, a noninflammatory condition *(Table 3)*.[4-7] Typically, patients with fibromyalgia have a subjective sense of swelling but no objective signs of synovitis. Fibromyalgia is suggested by the presence of polyarticular joint pain without synovitis, along with myalgias and tender points.[14]

Distribution

PATTERN

The pattern of joint involvement provides diagnostic clues. For instance, osteoarthritis of the hand usually involves the DIP and PIP joints, but not the metacarpophalangeal (MCP) joints.[15] Alternatively, rheumatoid arthritis of the hand most often involves the PIP and MCP joints, but not the DIP joints.[4,15] Psoriatic arthritis, crystal-induced arthritis, and sarcoidosis may affect all of these joints. Hand synovitis is distinctly unusual in chronic Lyme disease.[16]

Spondyloarthropathies typically involve the larger joints of the lower extremities. Osteoarthritis tends to spare wrists, elbows, and ankles, unless there is a history of trauma, inflammation, or a metabolic disorder such as hemochromatosis.

Depending on the underlying cause, the pattern of arthritis may change over time. For example, the acute stage of Lyme disease may include polyarticular arthralgias, whereas the chronic phase may include oligoarthritis, primarily in the knees.[17]

SYMMETRY

Joint involvement tends to be symmetric in systemic diseases such as rheumatoid arthritis, systemic lupus erythematosus, polymyalgia rheumatica, viral arthritides, and serum sickness reactions. Of eight variables examined in one study,[18] symmetric pain was the most potent discriminating feature for rheumatoid arthritis. Psoriatic arthritis, reactive arthritis, and gout are more likely to present with asymmetric peripheral involvement.[1,19,20]

Joint involvement tends to be symmetric in systemic diseases such as rheumatoid arthritis, systemic lupus erythematosus, and viral arthritides.

AXIAL INVOLVEMENT

Axial pain may be a helpful indicator in the evaluation of peripheral joint pain. In addition to peripheral joints, osteoarthritis may involve the lower back, the neck, or both. In contrast, rheumatoid arthritis is seldom an explanation for low back pain.

A young adult who presents with peripheral arthritis accompanied by the insidious onset of chronic low back pain and prolonged morning stiffness that improves with exercise probably has one of the spondyloarthropathies, such as ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease–associated arthropathy, or reactive arthritis.[21] Another common manifestation of spondyloarthropathies is enthesitis (inflammation of the muscular or tendinous insertions),[22] such as Achilles tendonitis or plantar fasciitis.[23] Dactylitis (inflammation of the finger or toe) is another classic sign of spondyloarthropathies; this condition, often referred to as "sausage digits," is caused by a combination of synovitis and enthesitis[22] *(Figure 2)*.

The rightsholder did not grant rights to reproduce this item in electronic media. For the missing item, see the original print version of this publication.

FIGURE 2.

TABLE 4
Selected Extra-Articular Manifestations Associated with Conditions That Result in Polyarticular Joint Pain*

Physical finding	*Diagnoses to consider*
Skin and mucous membranes	
Rash	
Erythema infectiosum	
Reticulated (lacy) rash	Human parvovirus B19 infection
Facial exanthem (slapped cheek)	Human parvovirus B19 infection
Malar rash	SLE, human parvovirus B19 infection, Lyme disease, rosacea, seborrhea, dermatomyositis
Plaques (scalp, navel, gluteal cleft)	Psoriasis
Heliotrope	Dermatomyositis
Erythema chronicum migrans	Lyme disease
Erythema marginatum rheumaticum	Rheumatic fever
Erythema nodosum	Sarcoidosis, Crohn's disease
Pyoderma gangrenosum	IBD, RA, SLE, anklyosing spondylitis, sarcoidosis, Wegener's granulomatosis
Palpable purpura	Hypersensitivity vasculitis, Schönlein-Henoch purpura, PAN
Livedo reticularis	Antiphospholipid-antibody syndrome, vasculitis, cholesterol emboli
Lesions	
Keratoderma blennorrhagicum	Reactive arthritis, psoriatic arthritis
Discoid skin lesions	Discoid lupus erythematosus, SLE, sarcoidosis
Gottron's papules or plaques	Dermatomyositis
Vesicopustule on erythematous base	Gonococcal arthritis
Eyes	
Iritis or uveitis	Spondyloarthropathies, sarcoidosis, Wegener's granulomatosis
Conjunctivitis	Spondyloarthropathies, SLE, Wegener's granulomatosis
Cytoid bodies (retinal exudates)	SLE
Scleritis	RA, relapsing polychondritis
Ischemic optic neuritis	Giant cell arteritis, Wegener's granulomatosis
Ears, nose, and throat	
Oral ulcers	SLE, Behçet's syndrome, reactive arthritis, Wegener's granulomatosis
Parotid enlargement	Sjögren's syndrome, sarcoidosis
Macroglossia	Amyloidosis
Scalp tenderness	Giant cell arteritis
Bloody or severe sinusitis	Wegener's granulomatosis
Inflammation of ear lobe	Relapsing polychondritis
Nails	
Onycholysis	Psoriatic arthritis, hyperthyroidism
Pitting	Psoriatic arthritis
Clubbing	IBD, Whipple's disease, hyperthyroidism
Nodules	RA, gout, Whipple's disease, rheumatic fever, amyloidosis, sarcoidosis
Tophi	Gout
Jaundice	Hepatitis, hemochromatosis
Hyperpigmentation	Whipple's disease, hemochromatosis

Physical finding	*Diagnoses to consider*
Skin and mucous membranes continued.	
Telangiectasia	Scleroderma
Thickened skin	Scleroderma, amyloidosis, eosinophilic fasciitis
Hair thinning	Hypothyroidism, SLE
Musculoskeletal system	
Tender points	Fibromyalgia
Heberden's nodes (DIP joints), Bouchard's nodes (PIP joints)	Osteoarthritis
Boutonnière and swan-neck deformities	RA, SLE, Ehlers-Danlos syndrome
Dactylitis ("sausage digits")	Spondyloarthropathies
Bursitis and enthesitis	Spondyloarthropathies
Constitutional conditions	
Fever	Bacterial or viral infection, Still's disease, subacute bacterial endocarditis, neoplasm
Bradycardia	Hypothyroidism
Cardiovascular system	
Mitral regurgitation and stenosis	Rheumatic fever
Aortic regurgitation	Ankylosing spondylitis, rheumatic fever, relapsing polychondritis, reactive arthritis, Marfan syndrome, Takayasu's arteritis
Cardiomyopathies	Viral infection, amyloidosis, sarcoidosis, SLE, polymyositis
New murmur, fever	Bacterial endocarditis, rheumatic fever
Diminished peripheral pulses	Giant cell arteritis, Takayasu's arteritis
Gastrointestinal system	
Splenomegaly	Felty's syndrome, tumor-associated arthritis
Hepatomegaly	Whipple's disease, hemochromatosis, amyloidosis, Wilson's disease
Positive fecal occult blood test	IBD
Genitourinary system	
Prostatitis	Reactive arthritis, ankylosing spondylitis
Urethritis or cervicitis	Reactive arthritis, gonococcal arthritis
Scrotal or vulvar ulcers	Behçet's syndrome
Hypogonadism	Hemochromatosis
Balanitis circinata	Reactive arthritis
Neurologic system	
Entrapment neuropathies	RA, hypothyroidism, hyperparathyroidism
Facial palsy	Lyme disease
Peripheral neuropathy	SLE, amyloidosis
Chorea	Antiphospholipid-antibody syndrome, SLE, rheumatic fever
Mononeuritis multiplex	RA, SLE, Lyme disease, vasculitis (e.g., PAN)
Seizures	SLE
Lymphadenopathy	Tumor-associated arthritis, SLE

SLE = systemic lupus erythematosus; IBD = inflammatory bowel disease; RA = rheumatoid arthritis; PAN = polyarteritis nodosa; DIP = distal interphalangeal; PIP = proximal interphalangeal.

**—The clues listed in this table are not, in themselves, diagnostic or complete; they are presented for illustrative purposes only.*

FIGURE 3.

A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues than classic rheumatologic laboratory tests.

Extra-Articular Manifestations

Extra-articular manifestations may provide clues to the presence of some rheumatologic diseases but, of themselves, are not diagnostic *(Table 4)*. For instance, extra-articular signs and symptoms can point to the likely reason for swollen PIP joints: a malar rash and oral ulcers indicate probable systemic lupus erythematosus *(Figure 3)*; proximal muscle weakness suggests polymyositis; and psoriatic skin and nail lesions raise the possibility of psoriatic arthritis.[24,25]

Similarly, in a patient with knee arthritis, the presence of conjunctivitis, oral ulcers, vesicopustules on the soles, or recent diarrhea may indicate reactive arthritis.[21,26] A history of erythema chronicum migrans and Bell's palsy points to the diagnosis of Lyme disease.[27] As a final example, a health care worker who presents with fever, a lacy rash, and symmetric joint pain (especially in the hands) may have erythema infectiosum caused by human parvovirus B19 infection.[28-30]

Disease Course

INTERMITTENT ARTHRITIS

When symptoms are present for a limited period (usually a few days to a month) and resolve completely before presenting again, crystal-induced arthritis (e.g., gout, pseudogout) is the likely diagnosis. Arthrocentesis should be considered during a symptomatic flare.[10,19,27,31] If synovial fluid analysis fails to identify crystals, palindromic rheumatism should be considered; this condition may progress to rheumatoid arthritis.

MIGRATORY ARTHRITIS

Migratory arthritis is characterized by rapid onset of swelling in one or two joints, with resolution over a few days. As the symptoms resolve, similar symptoms emerge in another joint, usually in an asymmetric location.[20,28] This symptom pattern can occur in gonococcal arthritis, rheumatic fever, sarcoidosis, systemic lupus erythematosus, Lyme disease, bacterial endocarditis, and Whipple's disease.[32]

Patient Demographics

GENDER

Before menopause, women are nine times more likely to develop systemic lupus erythematosus and three to four times more likely to develop rheumatoid arthritis.[20] After men and women reach 50 years of age, the gender difference for systemic lupus erythematosus and rheumatoid arthritis becomes less significant.[1]

Compared with men, women are nine times more likely to develop fibromyalgia. An estimated 60 percent of women with symptomatic human parvovirus B19 infection manifest arthropathy, whereas men with this infection appear to develop arthropathy much less often.[33,34] The gender ratio is more balanced for spondyloarthropathies and vasculitic conditions such as polyarteritis nodosa.

Gout usually presents about 20 years after puberty in men and about 20 years after menopause in women. This disease is rare in premenopausal woman, unless renal insufficiency is present.[10]

AGE

Certain diagnoses are more common in specific age groups. Rheumatic fever, systemic lupus erythematosus, rheumatoid arthritis, reactive arthritis, and spondyloarthropathies occur more often in younger persons. Osteoarthritis, polymyalgia rheumatica, and giant cell arteritis are more common in older persons.[13]

TABLE 5
Findings of Laboratory and Imaging Tests and Associated Conditions That Result in Polyarticular Joint Pain

Laboratory or imaging test	*Condition*
Complete blood count	
Anemia	Many inflammatory arthritides, especially SLE, RA, IBD, and human parvovirus B19 infection
Thrombocytopenia	SLE, human parvovirus B19 infection
Thrombocytosis	Acute-phase reaction, vasculitis, infection
Leukopenia	SLE, RA, Felty's syndrome, Sjögren's syndrome, human parvovirus B19 infection
Leukocytosis	RA, vasculitis, reactive arthritis, infection
Eosinophilia	SLE, RA, IBD, sarcoidosis, dermatomyositis, scleroderma, Churg-Strauss syndrome, PAN, eosinophilic fasciitis, cholesterol emboli
Chest radiograph	
Infiltrates or nodules	RA, sarcoidosis, Wegener's granulomatosis, Churg-Strauss syndrome
Serositis	SLE, RA
Upper lobe fibrosis	Ankylosing spondylitis
Diffuse fibrosis	RA, scleroderma, polymyositis
Rheumatoid factor	Healthy persons; RA, SLE, Sjögren's syndrome, sarcoidosis, reactive arthritis, PMR, polymyositis, psoriatic arthritis, endocarditis, chronic infections, cancer, chronic liver disease, many nonrheumatic causes
Joint aspiration	
Culture	Infection
Crystals	Gout, pseudogout
White blood cell count	Inflammation: > 2,000 per mm^3 (2×10^9 per L) Probable infection: > 50,000 per mm^3 (50×10^9 per L)
Inflammatory markers: elevated erythrocyte sedimentation rate or C-reactive protein (CRP)	Infection, most inflammatory arthritides, advanced age, PMR, giant cell arteritis, cancer, anemia, pregnancy; menses
Antinuclear antibody	Healthy persons; SLE, RA, scleroderma, Sjögren's syndrome, vasculitis, polymyositis, medications, many nonrheumatic causes
Hepatic transaminase: elevated aspartate transaminase or alanine transaminase	SLE, PAN, sarcoidosis, hemochromatosis, Sjögren's syndrome, infectious hepatitis, polymyositis
Urinalysis	
Hematuria	SLE, Wegener's granulomatosis, PAN
Proteinuria	SLE; Wegener's granulomatosis, amyloidosis
Elevated alkaline phosphatase	Bone metastases, Paget's disease, osteomalacia, PMR, ankylosing spondylitis, hyperparathyroidism
Electrocardiogram: atrioventricular block	Lyme disease, neonatal lupus, ankylosing spondylitis
Double-stranded DNA	SLE, especially lupus nephritis
Anti–SS-A (anti-Ro) and anti–SS-B (anti-La) antibodies	Sjögren's syndrome, SLE; healthy persons
HLA-B27	Healthy persons; spondyloarthropathies, reactive arthritis
Elevated uric acid	Gout, psoriatic arthritis, Paget's disease; healthy persons
False-positive VDRL	SLE, anticardiolipin antibody syndrome
Cytoplasmic antineutrophil cytoplasmic autoantibody (c-ANCA)	Wegener's granulomatosis
Elevated creatinine	SLE, Wegener's granulomatosis, vasculitis
Elevated creatine kinase (CPK)	Polymyositis, dermatomyositis, hypothyroidism
Elevated calcium	Hyperparathyroidism, cancer, sarcoidosis

SLE = systemic lupus erythematosus; RA = rheumatoid arthritis; IBD = inflammatory bowel disease; PAN = polyarteritis nodosa; PMR = polymyalgia rheumatica.

RACE

Polymyalgia rheumatica and Wegener's granulomatosis are more likely to affect whites.[13] In contrast, sarcoidosis and systemic lupus erythematosus are more common in blacks.

FAMILY HISTORY

Familial aggregation occurs in some arthritic diseases, such as spondyloarthropathies, rheumatoid arthritis, and Heberden's nodes of osteoarthritis.[1] There is a particularly strong association between ankylosing spondylitis and the HLA-B27 allele.

Laboratory Investigations

As previously noted, many rheumatologic laboratory tests must be interpreted in the context of the individual patient. For example, antinuclear antibody (ANA) tests are positive in 5 to 10 percent of the general population, a rate

TABLE 6
Categorization of Synovial Fluid

Categorization	*White blood cell count*	*Polymorphonuclear neutrophilic leukocytes*	*Examples*
Normal	0 to 200 per mm^3 (0 to 0.2 × 10^9 per L)	< 25% (0.25)	—
Noninflammatory	< 2,000 per mm^3 (2 × 10^9 per L)	< 25% (0.25)	Osteoarthritis, internal derangement, myxedema
Inflammatory	2,000 to 50,000 per mm^3 (2 to 50 × 10^9 per L)	> 75% (0.75)	Rheumatoid arthritis, psoriatic arthritis, gout, pseudogout, *Neisseria gonorrhoeae* infection
Septic	> 50,000 per mm^3 (50 × 10^9 per L); usually > 100,000 per mm^3 (100 × 10^9 per L)	Usually > 90% (0.90)	Septic arthritis (primary concern); occasionally, gout, pseudogout, reactive arthritis, Lyme disease

Information from reference 37.

that increases with age. Thus, given a one in 20 frequency for ANAs and a one in 2,000 frequency for systemic lupus erythematosus, only one in 100 persons with a positive ANA test will have the disease. Consequently, positive ANA test results must be interpreted with caution *(Table 3)*.[4-7] Given the high sensitivity of the currently used substrate for testing, a negative ANA test essentially rules out systemic lupus erythematosus.[1,5]

Spondyloarthropathies affect fewer than 1 percent of the general population. Indeed, patients who are HLA-B27 positive and do not have a family history of ankylosing spondylitis have only a 2 percent risk of developing this disorder.[35] Spondyloarthropathies can be overdiagnosed by relying only on a positive HLA-B27 test, because this test is positive in 8 percent of white persons.[35]

Rheumatoid factor testing lacks both sensitivity and specificity: the test is positive in 5 to 10 percent of the general population and negative in approximately 20 percent of persons with rheumatoid arthritis.[36] Therefore, both positive and negative rheumatoid factor test results must be interpreted cautiously. Indeed, rheumatoid factor testing is not useful when a patient lacks other diagnostic criteria for rheumatoid arthritis, especially synovitis.[36] The American Rheumatology Association's revised diagnostic criteria for rheumatoid arthritis use findings from the history, physical examination, and laboratory tests.[4] These criteria, which have been shown to be 91 to 94 percent sensitive and 89 percent specific, are useful for establishing a diagnosis of rheumatoid arthritis.[4,12,15]

A complete blood count, urinalysis, and a metabolic panel may provide more useful diagnostic clues than classic rheumatologic laboratory tests *(Table 5)*. For instance, hematuria, proteinuria, a low white blood cell (WBC) count, and thrombocytopenia may indicate the presence of systemic lupus erythematosus. Anemia with a low mean corpuscular volume may be a sign of underlying inflammatory bowel disease that is causing chronic gastrointestinal blood loss. Human parvovirus B19 infection can induce a decrease in the reticulocyte count, followed by anemia and, occasionally, leukopenia and thrombocytopenia.[30,34]

Synovial fluid analysis is performed primarily to diagnose infection or a crystal-induced arthritis. A synovial fluid WBC count of at least 2,000 per mm^3 (2 × 10^9 per L) suggests inflammation, whereas a count higher than 50,000 per mm^3 (50 × 10^9 per L) typically indicates synovial infection *(Table 6)*.[37] Fluid with a highly elevated WBC count or a predominance of neutrophils should be cultured to exclude infection.

Diagnostic Imaging

A number of radiographic findings are characteristic of specific rheumatic disorders. For instance, sacroiliitis is indicative of ankylosing spondylitis, erosions with periarticular osteopenia are typical of rheumatoid arthritis, and "pencil-in-cup" deformities are a sign of psoriatic arthritis. However, these radiographic findings take months to develop; early in the process, radiographs may be normal or show only nonspecific changes.

In early rheumatoid arthritis, magnetic resonance imaging demonstrates cartilage damage that is not evident on plain-film radiographs.[38] This damage highlights the importance of diagnosing rheumatoid arthritis early on the basis of the history and physical examination so that disease-modifying treatment can be initiated.

The authors indicate that they do not have any conflicts of interests. Sources of funding: none reported.

The authors thank Robert M. Wesley, M.A., project director for this series and director of research and program development for the Department of Family and Community Medicine at Southern Illinois University (SIU) School of Medicine, Springfield, for editing and commentary throughout development of the paper. The authors also acknowledge valuable suggestions from Rob Ewart, M.D., associate professor in the Department of Family and Community Medicine at SIU School of Medicine.

REFERENCES

1. Klinkhoff A. Rheumatology: 5. Diagnosis and management of inflammatory polyarthritis. CMAJ 2000;162:1833-8.
2. Sox HC Jr. Probability theory in the use of diagnostic tests. An introduction to critical study of the literature. Ann Intern Med 1986;104:60-6.
3. Woolf SH, Kamerow DB. Testing for uncommon conditions. The heroic search for positive test results. Arch Intern Med 1990;150: 2451-8.
4. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.
5. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
6. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [Letter]. Arthritis Rheum 1997;40:1725.
7. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33:160-72.
8. El-Gabalawy HS, Duray P, Goldbach-Mansky R. Evaluating patients with arthritis of recent onset: studies in pathogenesis and prognosis. JAMA 2000;284:2368-73.
9. Sood A, Panush RS, Pinals RS. Case management study: polyarthritis with fever. Bull Rheum Dis 1998;47(3):1-4.
10. Agudelo CA, Wise CM. Gout: diagnosis, pathogenesis, and clinical manifestations. Curr Opin Rheumatol 2001;13:234-9.
11. Scott DL, Houssien DA. Clinical and laboratory assessments in rheumatoid arthritis and osteoarthritis. Br J Rheumatol 1996; 35(suppl 3):6-9.
12. Grassi W, De Angelis R, Lamanna G, Cervini C. The clinical features of rheumatoid arthritis. Eur J Radiol 1998;27(suppl 1):S18-24.
13. Swannell AJ. Polymyalgia rheumatica and temporal arteritis: diagnosis and management. BMJ 1997;314:1329-32.
14. Reilly PA. The differential diagnosis of generalized pain. Baillieres Best Pract Res Clin Rheumatol 1999;13:391-401.
15. Sangha O. Epidemiology of rheumatic diseases. Rheumatology [Oxford] 2000;39(suppl 2):3-12.
16. Sigal LH. Musculoskeletal manifestations of Lyme arthritis. Rheum Dis Clin North Am 1998;24:323:51.
17. Steere AC. Diagnosis and treatment of Lyme arthritis. Med Clin North Am 1997;81:179-94.
18. La Montagna GL, Tirri R, Baruffo A, Preti B, Viaggi S. Clinical pattern of pain in rheumatoid arthritis. Clin Exp Rheumatol 1997; 15:481-5.
19. Hadler NM, Franck WA, Bress NM, Robinson DR. Acute polyarticular gout. Am J Med 1974;56:715-9.
20. Barth WF. Office evaluation of the patient with musculoskeletal complaints. Am J Med 1997;102(1A):3S-10S.
21. Gladman DD. Clinical aspects of the spondyloarthropathies. Am J Med Sci 1998;316:234-8.
22. McGonagle D, Gibbon W, Emery P. Classification of inflammatory arthritis by enthesitis. Lancet 1998;352:1137-40.
23. Krongard DF, DeVos D. Diagnosis of ankylosing spondylitis. Radiol Technol 1996;68:163-5.
24. Ross EL, D'Cruz D, Morrow WJ. Pathogenic mechanisms in psoriatic arthritis. Hosp Med 1998;59:534-8.
25. Gladman DD, Anhorn KA, Schachter RK, Mervart H. HLA antigens in psoriatic arthritis. J Rheumatol 1986;13:586-92.
26. Baldassano VF Jr. Ocular manifestations of rheumatic diseases. Curr Opin Ophthalmol 1998;9(6):85-8.
27. Wise CM, Agudelo CA. Diagnosis and management of complicated gout. Bull Rheum Dis 1998;47(4):2-5.
28. Pinals RS. Polyarthritis and fever. N Engl J Med 1994;330:769-74.
29. Woolf AD, Campion GV, Chishick A, Wise S, Cohen BJ, Klouda PT, et al. Clinical manifestations of human parvovirus B19 in adults. Arch Intern Med 1989;149:1153-6.
30. Young N. Hematologic and hematopoietic consequences of B19 parvovirus infection. Semin Hematol 1988;25:159-72.
31. Pittman JR, Bross MH. Diagnosis and management of gout. Am Fam Physician 1999;59:1799-806,1810.
32. Puechal X. Whipple disease and arthritis. Curr Opin Rheumatol 2001;13:74-9.
33. White DG, Woolf AD, Mortimer PP, Cohen BJ, Blake DR, Bacon PA. Human parvovirus arthropathy. Lancet 1985;1(8426):419-21.
34. Sabella C, Goldfarb J. Parvovirus B19 infections. Am Fam Physician 1999;60:1455-60.
35. Van der Linden SM, Valkenburg HA, de Jongh BM, Cats A. The risk of developing ankylosing spondylitis in HLA-B27 positive individuals. A comparison of relatives of spondylitis patients with the general population. Arthritis Rheum 1984;27:241-9.
36. Shmerling RH, Delbanco TL. How useful is the rheumatoid factor? An analysis of sensitivity, specificity, and predictive value. Arch Intern Med 1992;152:2417-20.
37. Klippel JH, Weyand CM, Crofford LJ, Stone JH, eds. Primer on the rheumatic diseases. 12th ed. Atlanta: Arthritis Foundation, 2001: 140-3.
38. Schweitzer M, Morrison WB. Arthropathies and inflammatory conditions of the elbow. Magn Reson Imaging Clin N Am 1997; 5:603-17.