20 Rheumatologic, Immunologic, & Allergic Disorders

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RHEUMATOLOGIC DISORDERS

Diagnosis & Evaluation

A. Examination of the Patient

Two helpful clinical clues for diagnosing arthritis are the **joint pattern** and **the presence or absence of extra-articular manifestations.** The joint pattern is defined by the answers to three questions: (1) Is inflammation present? (2) How many joints are involved? and (3) What joints are affected? Joint inflammation manifests as warmth, swelling, and morning stiffness of at least 30 minutes' duration. Overlying erythema occurs with the intense inflammation of crystal-induced and septic arthritis. Both the number of affected joints and the specific sites of involvement affect the differential diagnosis (Table 20–1). Some diseases—gout, for example—are characteristically monarticular, whereas other diseases, such as rheumatoid arthritis, are usually polyarticular. The location of joint involvement can also be distinctive. Only two diseases frequently cause prominent involvement of the distal interphalangeal (DIP) joint: osteoarthritis and psoriatic arthritis. Extra-articular manifestations such as fever (eg, gout, Still disease, endocarditis), rash (eg, systemic lupus erythematosus [SLE], psoriatic arthritis, Still disease), nodules (eg, rheumatoid arthritis, gout), or neuropathy (eg, polyarteritis nodosa, granulomatosis with polyangiitis narrow the differential diagnosis further.

B. Arthrocentesis and Examination of Joint Fluid

If the diagnosis is uncertain, synovial fluid should be examined whenever possible (Table 20–2). Most large joints are easily aspirated, and contraindications to arthrocentesis are few. The aspirating needle should never be passed through an overlying cellulitis or psoriatic plaque because of the risk of introducing infection. For patients who are receiving direct-acting oral anticoagulants or long-term anticoagulation therapy with warfarin, joints can be aspirated with a small-gauge needle (eg, 22F); the international normalized ratio (INR) should be less than 3.0 for patients taking warfarin.

1. Types of studies

A. Gross examination—Clarity is an approximate guide to the degree of inflammation. Noninflammatory fluid is transparent, mild inflammation produces translucent fluid, and purulent effusions are opaque. Bleeding disorders, trauma, and traumatic taps are the most common causes of bloody effusions.

B. Cell count—The synovial fluid white cell count discriminates between noninflammatory (less than 2000 white cells/mcL [2.0×10^9/L]), inflammatory (2000–75,000 white cells/mcL [2.0×10^9/L–75.0×10^9/L]), and purulent (greater than 100,000 white cells/mcL [100×10^9/L]) joint effusions. Synovial fluid glucose and protein levels add little information and should not be ordered.

C. Microscopic examination—Compensated polarized light microscopy identifies and distinguishes monosodium urate (gout, negatively birefringent) and calcium pyrophosphate (pseudogout, positive birefringent) crystals. Gram stain has specificity but limited sensitivity (50%) for septic arthritis.

D. Culture—Bacterial cultures as well as special studies for gonococci, tubercle bacilli, or fungi are ordered as appropriate.

2. Interpretation—Synovial fluid analysis is diagnostic in infectious or microcrystalline arthritis. Although the severity of inflammation in synovial fluid can overlap among various conditions, the synovial fluid white cell count is a helpful guide to diagnosis (Table 20–3).

DEGENERATIVE & CRYSTAL-INDUCED ARTHRITIS

DEGENERATIVE JOINT DISEASE (Osteoarthritis)

ESSENTIALS OF DIAGNOSIS

- A degenerative disorder with minimal articular inflammation.
- No systemic symptoms.
- Pain relieved by rest; morning stiffness brief.
- Radiographic findings: narrowed joint space, osteophytes, increased density of subchondral bone, bony cysts.

Table 20–1. Diagnostic value of the joint pattern.

Characteristic	Status	Representative Disease
Inflammation	Present	Rheumatoid arthritis, systemic lupus erythematosus, gout
	Absent	Osteoarthritis
Number of involved joints	Monarticular	Gout, trauma, septic arthritis, Lyme disease, osteoarthritis
	Oligoarticular (2–4 joints)	Reactive arthritis, psoriatic arthritis, inflammatory bowel disease
	Polyarticular (≥ 5 joints)	Rheumatoid arthritis, systemic lupus erythematosus
Site of joint involvement	Distal interphalangeal	Osteoarthritis, psoriatic arthritis (not rheumatoid arthritis)
	Metacarpophalangeal, wrists	Rheumatoid arthritis, systemic lupus erythematosus, calcium pyrophosphate deposition disease (not osteoarthritis)
	First metatarsal phalangeal	Gout, osteoarthritis

General Considerations

Osteoarthritis, the most common form of joint disease, is chiefly a disease of aging. Ninety percent of all people have radiographic features of osteoarthritis in weight-bearing joints by age 40. Symptomatic disease also increases with age. Sex is also a risk factor; osteoarthritis develops in women more frequently than in men.

This arthropathy is characterized by degeneration of cartilage and by hypertrophy of bone at the articular margins. Inflammation is usually minimal. Hereditary and mechanical factors may be involved in the pathogenesis.

Obesity is a risk factor for osteoarthritis of the knee, hand, and probably of the hip. Recreational running does not increase the incidence of osteoarthritis, but participation in competitive contact sports does. Jobs requiring frequent bending and carrying increase the risk of knee osteoarthritis (see Chapter 41).

Clinical Findings

A. Symptoms and Signs

Degenerative joint disease is divided into two types: (1) primary, which most commonly affects some or all of the following: the DIP and the proximal interphalangeal (PIP) joints of the fingers, the carpometacarpal joint of the thumb, the hip, the knee, the metatarsophalangeal (MTP) joint of the big toe, and the cervical and lumbar spine; and (2) secondary, which may occur in any joint as a sequela to articular injury resulting from either intra-articular (including rheumatoid arthritis) or extra-articular causes. The injury may be acute, as in a fracture; or chronic, as that due to occupational overuse of a joint or metabolic disease (eg, hyperparathyroidism, hemochromatosis, ochronosis).

The onset is insidious. Initially, there is articular stiffness, seldom lasting more than 15 minutes; this develops later into pain on motion of the affected joint and is made worse by activity or weight bearing and relieved by rest. Flexion contracture or varus deformity of the knee is not unusual, and bony enlargements of the DIP (Heberden nodes) and PIP (Bouchard nodes) are occasionally prominent (Figure 20–1). There is no ankylosis, but limitation of motion of the affected joint or joints is common. Crepitus may often be felt over the knee. Joint effusion and other articular signs of inflammation are mild. There are no systemic manifestations.

B. Laboratory Findings

Osteoarthritis does not cause elevation of the erythrocyte sedimentation rate (ESR) or other laboratory signs of inflammation. Synovial fluid is noninflammatory.

Table 20–2. Examination of joint fluid.

Measure	(Normal)	Group I (Noninflammatory)	Group II (Inflammatory)	Group III (Purulent)
Volume (mL) (knee)	< 3.5	Often > 3.5	Often > 3.5	Often > 3.5
Clarity	Transparent	Transparent	Translucent to opaque	Opaque
Color	Clear	Yellow	Yellow to opalescent	Yellow to green
WBC (per mcL)	< 200	< 2000	2000–75,000[1]	> 100,000[2]
Polymorphonuclear leukocytes	< 25%	< 25%	50% or more	75% or more
Culture	Negative	Negative	Negative	Usually positive[2]

[1]Gout, rheumatoid arthritis, and other inflammatory conditions occasionally have synovial fluid WBC counts > 75,000/mcL but rarely > 100,000/mcL.
[2]Most purulent effusions are due to septic arthritis. Septic arthritis, however, can present with group II synovial fluid, particularly if infection is caused by organisms of low virulence (eg, *Neisseria gonorrhoeae*) or if antibiotic therapy has been started.
WBC, white blood cell count.

Table 20–3. Differential diagnosis by joint fluid groups.

Group I (Noninflammatory) (< 2000 white cells/mcL)	Group II (Inflammatory) (2000–75,000 white cells/mcL)	Group III (Purulent) (> 100,000 white cells/mcL)	Hemorrhagic
Degenerative joint disease Trauma[1] Osteochondritis dissecans Osteochondromatosis Neuropathic arthropathy[1] Subsiding or early inflammation Hypertrophic osteoarthropathy[2] Pigmented villonodular synovitis[1]	Rheumatoid arthritis Acute crystal-induced synovitis (gout and pseudogout) Reactive arthritis Ankylosing spondylitis Rheumatic fever[2] Tuberculosis	Pyogenic bacterial infections	Hemophilia or other hemorrhagic diathesis Trauma with or without fracture Neuropathic arthropathy Pigmented villonodular synovitis Synovioma Hemangioma and other benign neoplasms

[1]May be hemorrhagic.
[2]Noninflammatory or inflammatory group.
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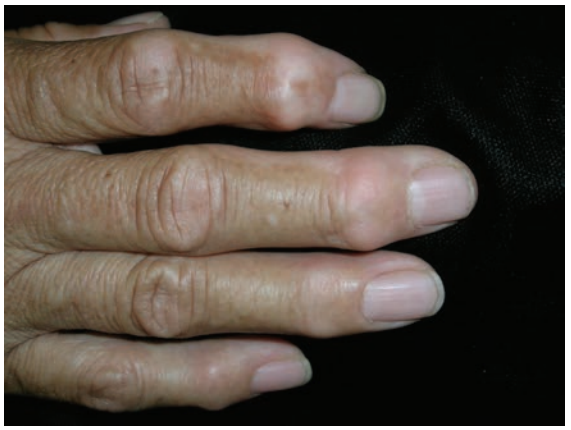
C. Imaging

Radiographs may reveal narrowing of the joint space; osteophyte formation and lipping of marginal bone; and thickened, dense subchondral bone. Bone cysts may also be present.

Differential Diagnosis

Because articular inflammation is minimal and systemic manifestations are absent, degenerative joint disease should seldom be confused with other arthritides. The distribution of joint involvement in the hands also helps distinguish osteoarthritis from rheumatoid arthritis. Osteoarthritis chiefly affects the DIP and PIP joints and spares the wrist and metacarpophalangeal (MCP) joints; rheumatoid arthritis involves the wrists and MCP joints and spares the DIP joints. Furthermore, the joint enlargement is bony-hard and cool in osteoarthritis but spongy and warm in rheumatoid arthritis. Skeletal symptoms due to degenerative changes in joints—especially in the spine—may cause coexistent metastatic neoplasia, osteoporosis, plasma cell myeloma, or other bone disease to be overlooked.



▲ **Figure 20–1.** Osteoarthritis in an older woman with Heberden nodes at the distal interphalangeal joints. There is some swelling beginning at the proximal interphalangeal joints creating Bouchard nodes. (Used, with permission, from Richard P. Usatine, MD.)

Prevention

Weight reduction reduces the risk of developing symptomatic knee osteoarthritis. Correcting leg length discrepancy of greater than 1 cm with shoe modification may prevent knee osteoarthritis from developing in the shorter leg. Maintaining normal vitamin D levels may reduce the occurrence and progression of osteoarthritis, in addition to being important for bone health.

Treatment

A. General Measures

Patients with osteoarthritis of the hand may benefit from assistive devices and instruction on techniques for joint protection; splinting is beneficial for those with symptomatic osteoarthritis of the first carpometacarpal joint. Patients with mild to moderate osteoarthritis of the knee or hip should participate in a regular exercise program (eg, a supervised walking program, hydrotherapy classes) and, if overweight, should lose weight. The use of assistive devices (eg, a cane on the contralateral side) can improve functional status.

B. Medical Management

1. Acetaminophen—Patients with mild osteoarthritis may benefit from acetaminophen (2.6–4 g/day orally). Growing awareness of the danger of hepatotoxicity from high doses of acetaminophen and clearer appreciation that its impact on pain is frequently neglible, acetaminophen is no longer recommended as first-line treatment for osteoarthritis of the hip or knee.

2. Topical therapies—Topical nonsteroidal anti-inflammatory drugs (NSAIDs) (eg, 4 g of diclofenac gel 1% applied to the affected joint four times daily) appear more effective

than placebo for knee and hand osteoarthritis and have lower rates of systemic side effects than with oral NSAIDs. Few studies have compared the efficacy of oral and topical NSAIDs. Because of their attractive safety profile, topical NSAIDs should be considered early in the treatment of patients with mild osteoarthritis affecting a few joints, especially of the hand or knee.

Topical capsaicin may be of benefit for osteoarthritis of the hand or the knee.

3. Oral NSAIDs—NSAIDs (see Table 5–7) are more effective than acetaminophen for osteoarthritis but have greater toxicity. NSAIDs inhibit cyclooxygenase (COX), the enzyme that converts arachidonic acid to prostaglandins. Prostaglandins play important roles in promoting inflammation, but they also help maintain homeostasis in several organs—especially the stomach, where prostaglandin E serves as a local hormone responsible for gastric mucosal cytoprotection. COX exists in two isomers—COX-1, which is expressed continuously in many cells and is responsible for the homeostatic effects of prostaglandins, and COX-2, which is induced by cytokines and expressed in inflammatory tissues. Most NSAIDs inhibit both isomers. Celecoxib is the only selective COX-2 inhibitor currently available in the United States.

Gastrointestinal toxicity, such as gastric ulceration, perforation, and gastrointestinal hemorrhage, are the most common serious side effects of NSAIDs. NSAIDs can also affect the lower intestinal tract, causing perforation or aggravating inflammatory bowel disease. The overall rate of bleeding with NSAID use in the general population is low (1:6000 users or less) but is increased by the risk factors of long-term use, higher NSAID dose, concomitant corticosteroids or anticoagulants, the presence of rheumatoid arthritis, history of peptic ulcer disease or alcoholism, and age over 70. *Proton pump inhibitors (eg, omeprazole 20 mg orally daily) reduce the incidence of serious gastrointestinal toxicity and should be used for patients with risk factors for NSAID-induced gastrointestinal toxicity.* Patients who have recently recovered from an NSAID-induced bleeding gastric ulcer appear to be at high risk for rebleeding (about 5% in 6 months) when an NSAID is reintroduced, even if prophylactic measures (such as proton pump inhibitors) are used. Compared with nonselective NSAIDs, celecoxib may be less likely in some circumstances to cause upper gastrointestinal tract adverse events.

All of the NSAIDs, including aspirin and celecoxib, can produce renal toxicity, including interstitial nephritis, nephrotic syndrome, prerenal azotemia, and aggravation of hypertension. Hyperkalemia due to hyporeninemic hypoaldosteronism is seen rarely. The risk of renal toxicity is low but is increased by the following risk factors: age older than 60 years, history of kidney disease, heart failure, ascites, and diuretic use.

All NSAIDs, except the nonacetylated salicylates and the COX-2 inhibitor celecoxib, interfere with platelet function and prolong bleeding time. Aspirin irreversibly inhibits platelet function, so the bleeding time effect resolves only as new platelets are made. In contrast, the effect of nonselective NSAIDs on platelet function is reversible and resolves as the drug is cleared. Concomitant administration of a nonselective NSAID can interfere with the ability of aspirin to acetylate platelets and thus may interfere with the cardioprotective effects of low-dose aspirin. *The FDA has warned that all NSAIDs can increase the risk of myocardial infarction and stroke in patients with or without risk factors for heart disease or known heart disease.* While the cardiovascular risk is related to the dose and duration of treatment, stroke and myocardial infarction can occur within the first week of treatment. Cardiovascular risks associated with naproxen, ibuprofen, and moderate dose celecoxib (200 mg orally daily) are comparable.

Chondroitin sulfate and glucosamine, alone or in combination, are no better than placebo in reducing pain in patients with knee or hip osteoarthritis.

4. Intra-articular injections—Many patients with moderately severe osteoarthritis of the knee who do not respond to NSAIDs receive intra-articular injections of corticosteroids, hyaluronate, or platelet-rich plasma. Although each of these can temporarily reduce pain, none has convincingly produced long-term benefits in reducing pain or preserving function. For example, a 2-year controlled trial demonstrated that injecting the knee with triamcinolone every 6 months was no more effective than injecting saline in reducing knee pain. The American College of Rheumatology does not recommend corticosteroid injections for osteoarthritis of the hand.

C. Surgical Measures

Total hip and knee replacements provide excellent symptomatic and functional improvement when involvement of that joint severely restricts walking or causes pain at rest, particularly at night. Arthroscopic surgery for knee osteoarthritis is ineffective.

Prognosis

Symptoms may be quite severe and limit activity considerably (especially with involvement of the hips, knees, and cervical spine).

When to Refer

Refer patients to an orthopedic surgeon when recalcitrant symptoms or functional impairment, or both, warrant consideration of joint replacement surgery of the hip or knee.

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