In the Clinic

Osteoarthritis

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CME Objective: To review current evidence for prevention, diagnosis, and treatment of osteoarthritis.

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What are the major risk factors for OA?

Although OA results from excessive mechanical stress, it is not an inevitable consequence of aging. A key role in OA development derives from predisposing factors. Disease susceptibility is influenced by genetic inheritance, age, race, ethnicity, and female sex (5). Age is the most important risk factor. With each advancing decade in the life spectrum, the incidence and prevalence of OA increase. Studies of twins have shown that 60%–70% of risk for OA results from genetic factors.

Sex is strongly related to OA at both the knee and hip joints—prevalence at these sites is nearly twice the rate in women as in men (1). At the hand joints, OA has strong female and genetic predilections and is similarly related to obesity, notwithstanding its distinction as a non–weight-bearing joint. This association of OA of the hand with obesity suggests that excess body weight exerts an effect via metabolic or cytokine-mediated influences and not biomechanical properties alone.

Although OA occurs worldwide, geographic and ethnic differences in population burden have been noted. For example, the prevalence of hand and knee OA is similar...
among Europeans and Americans. In contrast, prevalence of hip OA varies greatly, with markedly lower rates in African blacks, Asian Indians, and Chinese persons from Beijing and Hong Kong. Yet, older Chinese women in Beijing have a higher prevalence of knee OA than white women in the Framingham study (6).

Local mechanical factors, including malalignment, muscle weakness, and internal derangements, facilitate development and progression of OA (7, 8). Excessive joint loading can also be affected by obesity, joint injury, and occupations with repetitive bending (8, 9) and accentuate the likelihood of development or progression of OA.

As few as 5 degrees of genu varum (bow-legged) malalignment results in an estimated 70%–90% increase in compressive loading of the medial knee compartment (7). This corresponds to a 4-fold increase in the risk for worsening osteoarthritis of the medial knee over 18 months of follow-up (7). Conversely, genu valgum (knock-kneed) malalignment markedly increases compressive load on the lateral compartment of the knee, elevating the risk for lateral osteoarthritis progression 5-fold.

Should diet and physical activity be modified to prevent knee OA? Obesity is the single most important modifiable risk factor for incidence and progression of knee OA (5, 10-12). Across the United States, the prevalence of obesity has increased substantially in recent decades. Thus, a priority in the primary prevention of OA is to counsel overweight and obese patients to lose weight.

Among overweight women in the Framingham cohort, weight loss was associated with a significantly lower risk for knee OA. For every 11-lb weight loss, risk for OA decreased >50%, an effect that was more pronounced in women than in men (11).

Physical activity should be pursued in a manner that minimizes the potential for injury. Patients should be advised to use graduated training schedules and appropriate conditioning programs and to avoid intense loading of previously injured joints. Contact sports particularly seem to increase risk for meniscal tears and cruciate ligament injury, which are known to predispose to OA regardless of surgical repair (8, 13).

Quadriceps weakness decreases the ability of the muscle to distribute load across the joint and maintain joint stability. Moreover, weakness of the quadriceps may predate onset of knee OA and contribute to its development (14). Consequently, quadriceps muscle strengthening via exercise may diminish the risk for knee OA (15).

Prevention... Obesity is the single most important modifiable risk factor for knee OA. People participating in sports should be advised to engage in proper training and conditioning to avoid injury. All patients should be encouraged to exercise to maintain quadriceps strength.

CLINICAL BOTTOM LINE

What are the characteristic symptoms of OA? The insidious onset of activity-related joint pain frequently heralds OA (see the Box: Common Symptoms and Treatment of Osteoarthritis). An affected person with knee or hip involvement has pain with weight-bearing and ambulation, including stair-walking (3, 4). Lower-extremity joint pain arising from OA characteristically terminates with rest.

As the severity of osteoarthritic joint involvement progresses, so does the intensity of symptoms. As a result, affected persons with advanced OA may develop increasingly severe pain during previously well-tolerated activities (e.g., walking across a parking lot or stepping up into a home entranceway); nocturnal joint and rest pain usually signals the presence of advanced disease. Nocturnal OA pain needs to be distinguished from a microcrystalline arthropathy, occult cancer, or evolving infection (16).

What are the characteristic physical examination features?
When OA affects the knee joint, it characteristically produces crepitus, an audible and palpable grating quality when the knee is flexed and extended during physical examination (Table 1). Bony prominence is also a common finding, particularly

Similarly, osteoarthritic involvement at the thumb base and fingers is elicited by gripping and holding equipment, such as when lifting a heavy pot or writing or manipulating cutlery. Stiffness and swelling in an affected joint may be observed but is usually brief (lasting less than 30 minutes) and self-limited.
at the finger joints, where enlargement of the distal and proximal interphalangeal joints produces the characteristic eponymous Heberden and Bouchard nodes, respectively. Similar involvement at the base of the thumb produces squaring of the joint contour at the first carpometacarpal articulation.

To assess alignment, a goniometer can be used to visually bisect the thigh and lower leg along their lengths. The centers of both the patella and ankle should be located. The center of the goniometer is placed on the center of the patella, and the arms of this goniometer are extended along the center of the thigh and along the axis of the lower leg to the center of the ankle.

It is also important to remember that back and hip disorders can refer pain to the knee. Both of these anatomical sites should be evaluated to isolate the origin of the pain.

When should imaging studies be ordered?
Radiographs are notoriously insensitive to the early pathologic features of OA. As a result, the absence of supportive radiographic findings does not rule out symptomatic disease; however, positive radiographic findings also do not definitively diagnose OA. Other sources of pain, such as tendonitis or pes anserine bursitis at the knee and trochanteric bursitis at the hip, often contribute.

Over 50 years ago, Kellgren and Lawrence (17) developed diagnostic criteria for OA based on radiographic evidence of disease. Radiographic features include joint space narrowing, osteophyte (or spur) formation at the joint margin, cortical bone thickening (or eburnation), and formation of subchondral cysts. These radiographic features are shown in Figure 1, in which prominent asymmetric, or heterogeneous, joint space narrowing occurs at the medial femorotibial articulation. However, the width

![Figure](http://annals.org/)

**Figure.** Radiographic features of bilateral knee osteoarthritis showing medial joint-space narrowing (with varus deformities), bony sclerosis and osteophyte formation characteristic of osteoarthritis.
Table 2. Differential Diagnosis of Osteoarthritis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary osteoarthritis</td>
<td>Associated with age, presents with insidious onset of joint pain, often with stiffness and bony abnormalities. No strong inflammatory component. Differentiate from secondary causes, such as those due to systemic, metabolic, and inflammatory disorders</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>Secondary osteoarthritis due to iron overload, predominantly in men aged 40 to 60 y. Osteoarthritis in the second and third metacarpophalangeal joints with hook-like osteophytes are characteristic</td>
</tr>
<tr>
<td>Ochronosis</td>
<td>Early-onset lumbar spondylosis. Calcification and ossification of the lumbar intervertebral disks. Involves large joints and spares hands and feet</td>
</tr>
<tr>
<td>Multiple epiphyseal and spondyloepiphyseal dysplasia</td>
<td>Short stature, onset during teens to age 30. Mainly affects hips, knees, elbows, ankles, and shoulders. Radiographs show epiphyseal fragmentation and flattening of the femoral, metatarsal, and metacarpal heads with flattening and wedging of the thoracic and lumbar spine in patients with SED. Autosomal dominant pattern of inheritance</td>
</tr>
<tr>
<td>Calcium pyrophosphate</td>
<td>Chondrocalcinosis in knees, wrist, and symphysis pubis. Attacks of pseudogout. Osteoarthritis in the second and deposition disease third metacarpophalangeal joints. CPPD crystals may be identified in synovial fluid</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>Spine disease is common. 60% of patients have joint symptoms (knees, hips, shoulders, elbows). Soft-tissue swelling, widened distal phalanx tufts in hands without radiographic osteoarthritis. Radiography may show widened joint space followed later by typical features of osteoarthritis. Increased size of hands, feet, nose and jaw. Increased sweating and moist, coarsened skin. Glucose intolerance in 50%</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Synovial (soft-tissue swelling), not bony, enlargement of the proximal interphalangeal and metacarpophalangeal joints. Rarely involves the distal interphalangeal joints. Inflammatory signs (fatigue, prolonged stiffness). Rheumatoid nodules. Inflammatory synovial fluid. Marginal erosions and juxta-articular osteopenia seen on radiographs</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>Synovial and enthesal swelling. may involve distal interphalangeal joints. Dactylitis (sausage digits). Erosions and periostitis on radiography</td>
</tr>
<tr>
<td>Trochanteric bursitis</td>
<td>Pain and tenderness over the greater trochanter with normal hip range of motion. Pain may radiate down lateral aspect of thigh. Responds to local glucocorticoid injection</td>
</tr>
<tr>
<td>Anserine bursitis</td>
<td>Pain and tenderness over the anteromedial aspect of the lower leg below the joint line of the knee. Responds to local glucocorticoid injection</td>
</tr>
<tr>
<td>De Quervain tenosynovitis</td>
<td>Pain over the radial styloid and the base of the thumb due to inflammation of the abductor pollicis longus and extensor pollicis brevis. Provoked by pinching with thumb while moving wrist</td>
</tr>
<tr>
<td>Meniscal tear</td>
<td>Pain usually occurs acutely and is related to trauma. Associated with buckling and locking of the knee. Localized tenderness over the affected joint line. Effusions are often present and are usually hemarthroses</td>
</tr>
<tr>
<td>Positive McMurray test (clicking felt when knee is compressed and rotated during valgus or varus stress)</td>
<td></td>
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<tr>
<td>Osteonecrosis</td>
<td>Joint pain out of proportion to radiographic changes, often presents with acute or sub-acute hip or knee pain. Risk factors are high-dose corticosteroids, ethanol abuse, systemic lupus erythematosus, hemoglobinopathies. Diagnosis confirmed by MRI</td>
</tr>
<tr>
<td>Gout</td>
<td>Acute attacks of monoarthritis with joint erythema. Bony enlargement of joints may be present. Tophi typically present on examination. Radiographs show large erosions with overhanging edges and occasionally soft-tissue calcification of the tophus. If gout is suspected, fluid from the involved joints should be examined for crystals. Chronic tophaceous gout may involve the distal interphalangeal and proximal interphalangeal joints and first metatarsophalangeal joint causing angulation deformities and bony enlargement akin to osteoarthritis. Gout may develop in preexisting Heberden and Bouchard nodes</td>
</tr>
<tr>
<td>Neuropathic (Charcot) joint</td>
<td>May have severe osteoarthritis, with massive swelling or erythema but less pain than expected based on the appearance. Most commonly associated conditions are syringomyelia, diabetes, tabes dorsalis due to syphilis. With progression there is marked crepitus, instability, and palpable loose bodies. Radiographs show large unusually shaped osteophytes, transverse fractures, osteolysis, and large loose bodies. Synovial fluid is noninflammatory or bloody</td>
</tr>
<tr>
<td>Loss of pain sensation and proprioception ranges from mild to severe. Other associated conditions include meningomyelocele, leprosy, amyloidosis, and hereditary sensory neuropathies. Syringomyelia most often affects the shoulder followed by the elbow, wrist, and C-spine. The knee is most commonly affected in tabes dorsalis. The tarsal and tarsometatarsal joints are most often involved in diabetes</td>
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between the femoral condyle and tibial plateau is preserved at the lateral knee compartment. A bowlegged limb, or varus knee malalignment, is shown. The radiograph clearly demonstrates bilateral knee OA. In the general population, medial joint space narrowing, which is believed to be attributable to the center of gravity among humans during normal gait, predominates and generally is focused over the medial tibiofemoral joint space.

It should be noted that radiographic features often correlate poorly with clinical symptoms of OA. Thus, it is not uncommon for a patient with radiographic evidence of moderate OA to have few, if any, symptoms. By the same token, some patients with prominent symptoms have only mild radiographic changes. In clinical practice, OA should be diagnosed on the basis of history and physical examination (Table 1). Plain-film radiography confirms clinical suspicion and excludes other disorders.

Magnetic resonance imaging (MRI) is rarely indicated when the diagnostic suspicion for OA is high. However, it may be useful to evaluate for internal derangement of the knee, if clinically indicated (e.g., clinical symptoms of locking, instability or catching), or to detect early evidence of osteonecrosis. MRI is more sensitive than plain radiography in detecting areas of subchondral bone marrow edema, which correlate with symptoms of pain and with radiographic progression of OA (18, 19).

An unfortunate consequence of frequent use of MRI in clinical practice is excessive detection of meniscal tears. Meniscal pathology is nearly universal in persons with knee OA and not necessarily a cause of increased symptoms. A torn meniscus should not be removed unless it is contributing to joint locking or buckling (20).

When should clinicians perform diagnostic arthrocentesis?

Patients with OA can have periods of increased joint symptoms, or flares. At such times, there may be joint swelling and even some warmth or reddish discoloration. However, these examination findings are modest compared with features...
of rampant inflammatory arthritis (e.g., acute gout or septic arthritis).

When joint effusion is present, it is appropriate to perform diagnostic arthrocentesis, particularly if there is diagnostic uncertainty. Synovial fluid from osteoarthritic joints is relatively clear, viscous, and noninflammatory. Analysis demonstrates an elevated but noninflammatory white blood cell count (WBC), in the range of 200–2000 WBC/mm³.

In cases of red, hot, or swollen joints, diagnostic aspiration to look for possible septic arthritis, gout, and pseudogout should always be done. Under these circumstances, the synovial fluid specimen should always be sent for Gram stain and culture, leukocyte count, and crystal analysis.

Should other diagnostic studies be pursued in suspected cases?

Laboratory testing is not helpful to establish a diagnosis of OA. Because OA is relatively noninflammatory, complete blood count and acute-phase reactants should be normal. Obtaining creatinine level and liver function tests before initiating non-steroidal anti-inflammatory drug (NSAID) therapy, especially in elderly persons or those with comorbid conditions, should be considered to establish a baseline if iatrogenic features develop.

What are the diagnostic criteria?

When diagnosing OA of the knee, the physician should consider use of the criteria from the American College of Rheumatology (ACR), which are based on clinical, radiologic, and synovial fluid analysis data (21). Similar ACR criteria are available for classification of OA of the hip and hand joints (22, 23).

Are there distinct subsets?

OA is labelled as generalized OA when it simultaneously affects multiple joint groups in the appendicular (knees, hips, and small joints of the hands) and axial skeleton (cervical and lumbar spine).

OA can be subdivided as being primary or secondary. Secondary OA results from a well-defined cause, including a known injury (e.g., torn meniscus), metabolic disorder (e.g., hemochromatosis, Wilson disease, and ochronosis), the hypermobility syndrome, or endocrinopathy (e.g., acromegaly). It can also develop in joints previously damaged by infection (i.e., septic arthritis) or by an underlying inflammatory arthropathy (i.e., rheumatoid arthritis).

Erosive OA is a distinct subset that typically involves the hand joints and is predominant among women (24). Flares affecting the proximal and distal interphalangeal joints cause episodes of erythema, swelling, and severe pain. Radiographic evaluation may identify erosion of affected joints, together with osteophytes and ankylosis.

What is the differential diagnosis?

Alternative diagnoses for patients presenting with symptoms of OA are given in Table 2.

When should clinicians consult a rheumatologist or an orthopedist?

Referral for diagnostic consultation is advisable when the pattern of joint involvement is atypical, if the patient has symptoms that suggest inflammatory arthropathy, or in cases of severe manifestations. Such patients may not have OA but rather another type of arthritis, or they may have secondary OA.

Similarly, if a patient presents with features more consistent with a periarticular source of pain, such as pes anserine bursitis or trochanteric bursitis, consider referral to an orthopedist or rheumatologist if guidance is needed. A red, hot, and swollen joint requires prompt aspiration. If arthrocentesis cannot be obtained, seek specialist consultation right away.
Diagnosis... In clinical practice, OA should be diagnosed on the basis of history and physical examination. Plain-film radiographs are useful for diagnostic confirmation; diagnostic joint aspiration should be done to confirm suspicion of OA and to exclude other diagnoses (e.g., gout, pseudogout, septic arthritis) in atypical cases. MRI should be reserved to evaluate for internal derangement (e.g., joint locking, giving way).

What is the overall therapeutic approach to OA?
Management of OA should be tailored to the individual patient. Factors to consider in developing a treatment plan include the intensity of joint pain and severity of radiographic findings, as well as evidence of muscle weakness and malalignment. The presence of overweight and obesity warrants inclusion of weight loss goals among the therapeutic strategies.

A comprehensive approach necessitates discussion of a variety of treatment options and will often integrate family members regarding care, the primary goals of which are to diminish joint pain and enhance the functional capacity of the affected patient. Of note, treatment plans should not be defined rigidly by radiographic findings because the degree of joint space narrowing and number of osteophytes often correlate poorly with pain and functional assessment. Therefore, treatment should remain flexible and modified according to functional and symptomatic responses to a therapeutic trial.

Management should always begin with nonpharmacologic and nonsurgical strategies. This often involves a multidisciplinary approach, including physical therapists, occupational therapists, nutritionists, nurses, and physicians. Two major reasons substantiate this initial approach. First, there is a large body of evidence on the therapeutic efficacy of nonpharmacologic interventions. Second, pharmacologic interventions, particularly NSAID–related injury to the gastrointestinal, renal, and central nervous systems, have the potential for toxicity.

Pharmacologic agents should be offered only when more conservative efforts have failed to improve function. Many prescription and over-the-counter agents are available for medical management of OA. Surgery should be a last resort.

Therapeutic guidelines from professional organizations addressing the management of OA should be consulted. These documents are based on evidence from trials; expert consensus supports this approach (25-31).

How does education fit into the patient–physician discussion?
Education should be an integral part of treatment for any chronic disease and can favorably affect disease outcomes. Patients with OA should be encouraged to participate in self-management programs, such as those conducted by the Arthritis Foundation, or to consult videos, pamphlets, and newsletters. These media provide useful information about the natural history of disease, resources for social support, and instructions on coping skills (32).

Notably, although education programs have often served as a control group in exercise intervention trials, patient education interven-
tions have themselves shown therapeutic benefit in OA management.

**Is weight loss part of the treatment plan for knee OA?**

Absolutely! Overweight and obese patients with OA of the knee joint should be encouraged to lose weight through a combination of diet and exercise.

Among 316 community-dwelling overweight and obese adults who participated in the Arthritis, Diet and Activity Promotion Trial (ADAPT), those assigned to an 18-month program of exercise and a calorie-restricted diet showed a 24% improvement in physical function and a 30% decrease in knee pain. These improvements were far superior to those observed on patients assigned to exercise or diet only (33).

Most recently, among 454 overweight and obese community-dwelling adults enrolled in the Intensive Diet and Exercise for Arthritis (IDEA) trial, over an 18-month intervention period those assigned to the diet-plus-exercise group and those assigned to the diet-intervention group alone had greater weight loss than that of persons in the exercise-only group (34). Mean weight loss was greater with diet-plus-exercise group (10.6 kg) than among the diet- (8.9 kg) or exercise-only (1.8 kg) group.

**What is the role of exercise in the management of OA of the knee or hip?**

An exercise program, whether conducted in a group setting or at home, is a critical component of OA management. Exercise increases aerobic capacity, muscle strength, and endurance and facilitates weight loss (35). Patients with OA who can exercise should be encouraged to participate in a low-impact aerobic exercise program, such as walking, biking, or swimming (36). Aerobic walking and quadriceps-strengthening exercises reduce pain and increase function (37). The buoyant nature of water makes aquatic exercise a particularly attractive option for patients with poor tolerance of exercise on an unyielding surface (38).

Exercise programs should be individualized. Strategies to improve adherence (e.g., long-term monitoring), the main predictor of long-term outcome, should be adopted. Exercise that the patient enjoys is more likely to be sustained. Of note, some forms of exercise, particularly those of high velocity and high impact, can be harmful to an already-compromised osteoarthritic joint. Such activities as running and step aerobics should be discouraged.

The Fitness Arthritis and Seniors Trial (FAST) demonstrated that among 439 community-dwelling adults with radiographically defined OA, both an aerobic exercise program and resistance exercise program showed greater improvement in physical disability scores, knee pain scores, 6-minute walk test times, times to climb and ascend stairs, to lift and carry 10 pounds, and getting in and out of a car than did the comparison health education group (35).

**When should clinicians prescribe physical and occupational therapy?**

Physical therapy is an excellent option for improving joint biomechanics in the patient with knee or hip OA. The physical therapist can instruct the patient in active and passive range-of-motion exercise, muscle strengthening, and joint-protection principles. Physical therapy can help strengthen periarticular muscles (i.e., quadriceps) and improve alignment, reducing the stress borne by the osteoarthritic knee and diminishing joint pain.

A randomized, controlled trial compared manual therapy (passive, physiologic, and accessory joint movements; muscle stretching; and soft tissue mobilization) and a standardized knee exercise program with subtherapeutic ultrasonography. The average distance walked in 6 minutes at 8 weeks among patients in the treatment group was 170 m more than in the placebo group; average Western Ontario and McMaster Universities (WOMAC) scores were 599 mm higher. At 1 year, patients in the treatment group achieved clinical and statistical improvement (39).
Similarly, occupational therapy is a key resource in management of OA of the hand. Referred patients may benefit from range-of-motion exercises, joint protection instruction, and splinting of the first carpometacarpal joint.

Is there a role for assistive devices? Among persons affected by knee OA, improvement in stability and diminished pain on ambulation can frequently be achieved by use of a cane. Canes and other assistive devices (e.g., walker) work by unloading the knee (or hip), resulting in improved gait and mobility and diminished pain.

Instruction in proper use of a cane is warranted. Counsel patients to place the cane in the hand contralateral to the predominantly affected knee (or hip), thereby shifting the body's weight over to the cane. This maneuver enables the body's weight to be transferred away from the structurally compromised osteoarthritic limb.

When navigating stairs, the patient should be advised to ascend each stair, one at a time, while advancing with the good (unaffected) limb first; in contrast, when descending a flight of stairs one step at a time, the affected limb descends ahead of the unaffected side. During both the ascent and descent of stairs, the cane (and the body's weight on it) advances when the affected osteoarthritic limb is brought forward.

Adaptive devices are also beneficial for hand OA. Large-grip utensils, writing instruments, and key holders reduce force across osteoarthritic fingers and the base of thumb joints while enhancing the gripping motion and reducing pain.

What is the role of lateral-wedge insoles?
In the context of knee OA with predominant unilateral involvement, unloading the narrowed (e.g., medial tibiofemoral) compartment may be pursued with a variety of approaches, including an unloading brace and lateral shoe wedges. The intent of these devices is to transfer load from the narrowed to the more open knee compartment, thereby alleviating knee pain. Supportive evidence for these measures is conflicting.

Recently, a meta-analysis integrated data from 12 randomized trials to evaluate whether lateral wedge insoles reduced patient-reported pain (40). Shoe-based treatments consisting of lateral heel wedge insoles or shoes with variable stiffness soles aimed at reducing medial knee load were compared with neutral or no-wedge-control conditions among patients with painful medial knee OA. The pooled standardized differences suggested a favorable association with lateral wedges than with control; however, heterogeneity was substantial. Although meta-analytic pooling of these studies showed a statistically significant association between lateral wedges and reduced pain, restriction to studies that used a neutral insole comparator did not show a clinically important association. Larger trials with a lower risk of bias suggested a null association.

Which analgesic agents should clinicians prescribe first?
There are several recommended first-line agents for OA, depending on the comorbid conditions, age, and level of pain. Acetaminophen in doses up to 4 g/day is often the first choice for mild to moderate pain associated with OA. Advocacy for its front-line role stems from comparable efficacy to NSAIDs with a safer gastrointestinal profile. The Appendix Table (available at www.annals.org) presents pharmacologic treatment options for OA.

NSAIDs may be added or substituted in patients who respond inadequately to acetaminophen.

NSAIDs are also considered by many physicians to be the preferred first-line agents in medical management of OA (41). However, routine use of NSAIDs in osteoarthritis has disadvantages. All NSAIDs, both nonselective and cyclo-oxygenase (COX)-2-selective, are associated with significant potential toxicity, particularly among the elderly. This toxicity contributes to a substantial volume of hospitalizations and deaths each year in the United States (42). COX-2-selective and nonselective NSAIDs should be prescribed with caution in light of concern regarding cardiovascular risk (43).

**When are topical analgesics useful?**

Topical NSAIDs have been found to be effective in relieving pain when compared with placebo for both OA of the hand and knee joints (44). An attractive feature of this approach is reduced adverse gastrointestinal reactions by maximizing local delivery and minimizing systemic toxicity. Although these topical agents can be associated with local side effects, such as rash, itching, and burning, they are usually minimal. These medications are attractive first-line agents for patients wishing to avoid systemic therapy.

Topical capsaicin, an active ingredient of chili peppers that modulates nociceptive fibers, can be used as an alternative to systematic pharmacologic therapy. Capsaicin is applied over the affected knee and hand joints. There are two dosing concentrations available; capsaicin in a concentration of 0.025% is better tolerated than 0.075%, and should be applied 3–4 times per day for at least 3–4 weeks.

**What are the best strategies for avoiding drug toxicity when prescribing NSAIDs, especially to high-risk groups?**

Patients at high risk for peptic ulcer disease or gastrointestinal bleeding include persons older than 65 years, those taking anticoagulants, and those with comorbid medical conditions or a history of peptic ulcer disease or gastrointestinal bleeding.

Among these high-risk groups, nonselective NSAIDs plus a gastroprotective agent, or a COX-2-selective inhibitor, should be used. These approaches have a similar gastrointestinal safety profile (45).

A meta-analysis of 26 studies comparing dyspepsia between COX-2 inhibitors and NSAIDs revealed a 12% relative risk reduction for COX-2 inhibitors with an absolute risk reduction of 3.7% (45).

Concomitant use of low-dose aspirin, a common cardioprotective approach, may partially abrogate the protective gastrointestinal effect of the COX-2 inhibitors (46). Similarly, ibuprofen, when administered before aspirin, may limit aspirin’s cardioprotective effect as assessed by serum thromboxane B2 formation and platelet aggregation (47).

Caution should be exercised when COX-2 inhibitors and certain NSAIDs are used in patients with cardiac risk factors (43). Evidence suggests that patients with cardiovascular disease who must take NSAIDs should be offered antiplatelet agents when there are no contraindications.

Other medications, such as tramadol and duloxetine, can also be considered.

Opiates are can be used for patients who have no other appropriate medical or surgical options.
When are intra-articular glucocorticoids or hyaluronic acid indicated?

Intra-articular glucocorticoids are effective at improving pain and function in the context of knee OA but their benefit is generally short-term (about 1 wk) (48). Intra-articular steroids should not be used more than once every 4 months because repeated use can cause cartilage and joint damage, resulting in disease progression.

Hyaluronic acid is a high-molecular-weight polysaccharide found in the extracellular matrix of connective tissue. Symptomatic benefit after injection of hyaluronic acid is equivalent to that achieved from arthrocentesis (49). There are no data supporting the use of one preparation over another. Further, meta-analyses of the efficacy of hyaluronic acid do not agree completely, suggest that the effects are moderate although more durable than intra-articular steroids, emphasize that evidence is heterogeneous, and have found a significant placebo response.

What is the role of glucosamine-chondroitin and acupuncture?

Glucosamine and chondroitin compounds have attracted a great deal of attention. However, recent meta-analyses on glucosamine and one on chondroitin point out the limitations of available studies (50). The symptom-modifying effect of these agents is similar to placebo; their potential structure-modifying benefits are uncertain.

The Glucosamine/Chondroitin Arthritis Intervention Trial assessed the efficacy of glucosamine and chondroitin sulfate, alone and combined, and found them to be equivalent to placebo in persons with knee OA (51).

OA is a leading medical condition for which alternative therapies are used. Acupuncture, as a form of complementary therapy, may relieve pain and improve function, but the data are equivocal.

A total of 9 randomized trials, each longer than 6 weeks in duration, compared needle acupuncture with a sham, usual care, or waiting list control, for knee OA and were integrated into a meta-analysis (52). Patients who received acupuncture reported clinically relevant short- and long-term improvements in pain and function compared with patients in usual care control groups. However, when aggregated over a large number of clinical trials, therapeutic benefit, in terms of both pain and functional outcomes, was modest.

When should clinicians consider joint lavage, debridement, or joint replacement?

Surgery should be reserved for patients in whom symptoms are refractory to medical therapy. Typical indications for surgery are debilitating pain and major limitations in such functions as walking, working, or sleeping.

There is no role for joint lavage or arthroscopic debridement in the treatment of knee OA. Several large, randomized, methodologically rigorous studies have examined the role of these modalities in knee OA, both with and without concomitant meniscal tears (20, 53, 54). Across these reports, neither arthroscopic intervention offered therapeutic benefit at 6 months, or at 1 or 2 years, postoperatively, in relation to a sham surgical procedure or an exercise control. By far the most common indication for knee and hip replacement surgery is OA; however, there are no clear-cut standards indicating who should receive joint replacement. In fact, even levels of pain and functional disability do not reliably predict which patients surgeons consider appropriate for replacement surgery (55).

Referral for joint replacement should only be considered after an adequate trial of conservative therapy in patients who have moderate to severe symptoms that significantly affect quality of life.
Treatment... The overarching goal of OA treatment is to alleviate pain and improve functional capacity. Primary care for OA should emphasize nonpharmacologic treatments, including weight loss, exercise, and physical therapy. Only when more conservative efforts fail to improve function should pharmaceutical options be offered. Acetaminophen is a common first-line approach for mild pain. NSAIDs should be used with caution with due attention to potential side effects. Surgery should be reserved for patients with advanced disease and intractable symptoms refractory to medical therapy.

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Information on osteoarthritis from the National Institutes of Health MedlinePlus, including an interactive tutorial in English and Spanish.
www.cdc.gov/Features/OsteoarthritisPlan/
www.cdc.gov/arthritis/pa_overview.htm
Information on osteoarthritis from the Centers for Disease Control and Prevention, including information on physical activity and arthritis.
www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/osteoarthritis.asp
Information on osteoarthritis from the American College of Rheumatology.

Clinical Guidelines
www.rheumatology.org/Practice/Clinical/Guidelines/Osteoarthritis_%28Members__Only%29/
Recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee from the American College of Rheumatology in 2012.
www.aaos.org/research/guidelines/TreatmentofOsteoarthritisoftheKneeGuideline.pdf
http://guidance.nice.org.uk/CG99

Diagnostic Tests and Criteria
www.rheumatology.org/practice/clinical/classification/oknee.asp
www.rheumatology.org/ACR/practice/clinical/classification/oa-hand/oshand.asp
Classification criteria for osteoarthritis of the knee, hand, and hip from the American College of Radiology.
THINGS YOU SHOULD KNOW ABOUT OSTEOARTHITIS

What is osteoarthritis?
- A degenerative joint disease that causes cartilage to break down.
- Without cartilage, your bones start to rub together, and over time this can permanently damage the joint.
- Osteoarthritis causes pain, swelling, and reduced motion in your joints.
- It can occur in any joint but usually it affects your hands, knees, hips or spine.

What are risk factors for osteoarthritis?
- Getting older.
- Being a woman.
- Bone deformities, such as malformed joints or defective cartilage.
- Joint injuries, such as from playing sports or from an accident.
- Being overweight, which puts added stress on your weight-bearing joints.
- Working in an occupation that places repetitive stress on a particular joint.
- Having diabetes, underactive thyroid, gout, or Paget disease of bone.

How is it treated?
- Keep as active as you can.
- Do the exercises you and your doctor agree are right for you. Go to physical therapy if you need to.
- If you are too heavy, try to lose weight. Ask your doctor for help.
- Use canes, braces, and other aids to make it easier to get around.
- To reduce pain, your doctor may recommend pain relievers, cortisone shots, or lubrication injections.
- Surgery may be used to realign bones or to replace joints.
- Call your doctor if you have fever; red, hot, or swollen joints; more pain than usual; or falls.

What questions should you ask your doctor?
- Which medicines are best to treat my pain?
- Are there side effects? If so, what are they?
- What do I do if my medicines stop working?
- Will shots into my joints help?
- Will I need surgery on my joints?

For More Information

www.arthritis.org/conditions-treatments/disease-center/osteoarthritis/
www.arthritisnow.org/osteoarthritis/
Information on osteoarthritis and other resources from the Arthritis Foundation, including exercise videos.

www.niams.nih.gov/Health_Info/Osteoarthritis/default.asp
Handout on osteoarthritis from the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

http://nihseniorhealth.gov/osteoarthritis/treatmentandresearch/video/arth4_na_intro.html
http://nihseniorhealth.gov/osteoarthritis/treatmentandresearch/video/arth3_na_intro.html
Videos on how exercises can help and on using assistive devices from NIH Senior Health.
1. A 68-year-old woman is evaluated for a 10-year history of left knee pain associated with osteoarthritis. She is limited in ambulation to two blocks and now has pain at rest, which also disturbs her sleep. She reports only partial relief with NSAIDs and now takes hydrocodone on a regular basis. She has had little benefit from physical therapy or intra-articular corticosteroid injections. She has no other pertinent personal medical history.

On physical examination, temperature is 37.2°C (99.0°F), blood pressure is 142/72 mm Hg, pulse rate is 88/min, and respiration rate is 18/min. BMI is 28. The left knee is enlarged. Range of motion of the knee elicits significant crepitus with medial joint line pain. There is no varus or valgus laxity or anterior or posterior laxity.

Radiographs of the knee reveal severe joint-space narrowing of the medial compartment of the joint and mild to moderate narrowing of the patellofemoral joint. There is a tibial osteophyte and subchondral sclerosis.

Which of the following is the most appropriate treatment for this patient?

A. Arthroscopic lavage  
B. High tibial osteotomy  
C. Hyaluronate injection  
D. Total knee replacement

Which of the following is the most appropriate treatment for this patient?

A. Celecoxib  
B. Colchicine  
C. Indomethacin  
D. Prednisone  
E. Tramadol

3. A 65-year-old woman is evaluated for a 3-month history of left knee pain of moderate intensity that worsens with ambulation. She reports minimal pain at rest and no nocturnal pain. There are no clicking or locking symptoms. She has tried naproxen and ibuprofen but developed gastrointestinal symptoms. She is anemic and her hemoglobin level is 12 g/dL. CT scan of the knee reveals small effusions bilaterally, with crepitsus and tenderness along the medial joint line.

Laboratory studies, including complete blood count, erythrocyte sedimentation rate, plasma glucose, and serum creatinine, are normal.

Radiographs of the knees, including weight-bearing studies, reveal bilateral medial joint-space narrowing, subchondral sclerosis, and small osteophytes.

Which of the following is the most appropriate treatment for this patient?

A. Celecoxib  
B. Colchicine  
C. Indomethacin  
D. Prednisone  
E. Tramadol

4. A 52-year-old woman is evaluated for a 5-year history of gradually progressive left knee pain. She has 20 minutes of morning stiffness, which returns after prolonged inactivity. She has minimal to no pain at rest. She reports no clicking or locking of the knee. Over the past several months, the pain has limited her ambulation to no more than a few blocks.

On physical examination, vital signs are normal. BMI is 25. The left knee has a small effusion and some fullness at the back of the knee; the knee is not erythematous or warm. Range of motion of the knee elicits crepitus. There is medial joint line tenderness to palpation, bony hypertrophy, and a moderate varus deformity. There is no evidence of joint instability on stress testing.

Radiographs of the knee reveal bone-on-bone joint-space loss and numerous osteophytes.

Which of the following is the most appropriate next diagnostic step for this patient?

A. Computed tomography of the knee  
B. Joint aspiration  
C. Magnetic resonance imaging of the knee  
D. No diagnostic testing

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CORRECTION

Correction: In the Clinic: Osteoarthritis

In a recent In the Clinic (1), the sentence in the first paragraph on page ITC1-5 should read as follows: "Bony prominence is also a common finding, particularly at the finger joints, where enlargement of the distal and proximal interphalangeal joints produces the characteristic eponymous Heberden and Bouchard nodes, respectively."

This has been fixed in the online version.

Reference