EMERGENCY MEDICINE REPORTS

Practical, Evidence-Based Reviews in Emergency Care

MAY 3, 2015 VOL. 36, NO. 10

AUTHORS:

Terrence C. Tan, DO, Rheumatology Fellow, Loma Linda University, Loma Linda, CA.

Zahra Shahim, MD, Medicine Resident, Loma Linda University, Loma Linda, CA.

Keith K. Colburn, MD, FACP, FACR, Professor of Medicine, Chief of Rheumatology, Loma Linda University and Loma Linda VA Medical Center, Loma Linda, CA.

PEER REVIEWER:

Robert A. Hawkins, MD, FACR, Associate Professor of Medicine, Wright State University, Dayton, OH; Associate Residency Program Director, Internal Medicine Residency Program, Kettering Medical Center, Kettering, OH.

STATEMENT OF FINANCIAL DISCLOSURE

To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Farel (CME question reviewer) owns stock in Johnson & Johnson. Dr. Stapczynski (editor) owns stock in Pfizer, Johnson & Johnson, AxoGen, Walgreens Boots Alliance Inc., and Bristol Myers Squibb. Ms. Mark's spouse (executive editor) works for a company that creates advertising for Uroplasty. Dr. Schneider (editor), Dr. Colburn (author), Dr. Tan (author), Dr. Shahim (author), Dr. Hawkins (peer reviewer), Dr. Wise (editor), and Mr. Landenberger (editorial director) report no financial relationships with companies related to the field of study covered by this CME activity.

AHC Media

Osteoarthritis

Osteoarthritis does not seem initially like a topic that has much relevance to emergency medicine. After all, what is acute or emergency about it? In reality, as we all know, patients come to the ED with undifferentiated symptoms, including joint pain. Many times, this joint pain is due to undiagnosed osteoarthritis. When I tell patients this is what they have, they have many questions in return. After reading this article, I feel better able to answer these questions. I also feel more confident in my initiation and adjustment of the NSAIDs used in treating these patients.

—J. Stephan Stapczynski, MD, FACEP, Editor

Introduction

Osteoarthritis (OA) can be described as the failed repair of damage that has been caused by excessive mechanical stress (defined as force/unit area) on joint tissues.[1] This implies that although multiple factors may lead to OA, mechanical impact (either as a major single event or as repetitive micro trauma) is central to all of these. Also known as osteoarthrosis or degenerative joint disease, OA is the most important chronic musculoskeletal disorder in humans.

Although not a life-threatening disease, OA is considered one of the major concerns in human health care because of the vast number of people involved and the severe impact this literally crippling disease can have on quality of life.

Contribution of Osteoarthritis to Functional Limitations and Disability

Arthritis is the leading cause of disability among adults,[2-10] and there is no question that OA in particular is related to disability as adults age. The risk of OA increases with age, so that by the age of 80 years, radiographic evidence of joint degeneration is found in nearly everyone.[11]

OA pathology results in the degeneration of cartilage, bone, and soft tissues integral to joints, most commonly the hand, knee, hip, spine, and foot. Although OA is associated with joint-related symptoms such as pain and stiffness, there is wide variation in symptoms for those with radiographic evidence of joint degeneration changes, and many with radiographic changes report no pain.[12]

Pathogenesis

One of the main mechanisms for the development of OA is damage to the articular cartilage by trauma, which in turn causes chondrocytes to release degradative enzymes leading to abnormal repair of the matrix.[13-16] This in turn causes the subsequent development of OA. Cartilage from osteoarthritic joints is thought to deform more easily compared to normal joint tissue in response to the same mechanical load.[17]

Chondrocytes maintain homeostasis of the articular cartilage by synthesizing

EXECUTIVE SUMMARY

- Osteoarthritis (OA) is one of the most common reasons for patients to seek attention from a physician. It is also one of the most common chronic diseases that play such a devastating role in cost and disability.
- The pathogenesis of OA is quite complex, involving altered chondrocyte homeostasis with abnormal matrix repair, influence of osteoblasts, proteases, and certain cytokines.
- Although the underlying cause is unknown, almost everyone has some symptoms by age 70, with women being more commonly affected after age 55.
- Common differential diagnoses include calcium pyrophosphate crystal deposition disease, rheumatoid arthritis, and infectious monoarticular disease.
- Major radiographic findings of OA include joint space narrowing, subchondral sclerosis, osteophytes, and subchondral cysts.
- Pharmacologic options for treatment include analgesics, opioids, oral and topical NSAIDs, and intraarticular glucocorticoid injections.

collagens, proteoglycans, and proteinases. OA develops when there is failure of these chondrocytes to maintain this homeostasis between synthesis and degradation.

Osteoblasts also play a role in the formation of OA. These osteoblasts in OA patients produce more alkaline phosphatase, osteocalcin, insulin-like growth factor, and urokinase in comparison to normal osteoblasts leading to degradation of the cartilage matrix.

Certain cytokines such as IL-1, tumor necrosis factor alpha, insulin-like growth factor, transforming growth factor-beta, and interleukin-6 were shown to play a role in OA. There is an increased level of IL-1 in the joints of patients with knee OA compared to those without OA. Tumor necrosis factor alpha is increased in the joints of OA patients.[18] Insulin-like growth factor increases cartilage and matrix synthesis, and is decreased in the joints of OA patients. Another cytokine known to maintain cartilage, called transforming growth factor-beta, is found in low levels in osteoarthritic joints.[19] Interleukin-6 has a complex role in OA. This cytokine, which is a modulator in cartilage remodeling and degradation, was shown to be increased in osteoarthritic joints, to increase TNF receptors (which causes breakdown of cartilage), and to increase the production of tissue metalloproteinase-1 (which inhibits breakdown of cartilage).

Nitric oxide also plays a role in the pathogenesis of OA. In OA patients, nitric oxide is produced in the joints in large amounts. Nitric oxide is partly responsible for blocking glycosaminoglycan and collagen synthesis by IL-1 and activating metalloproteinases.

The risk of OA progression increased three-fold in patients with low vitamin D intake.[20] However, low intake and serum levels of vitamin D did not increase the risk for developing OA.

Etiology, Incidence, and Risk Factors

OA is a normal result of aging.[21] It is also caused by "wear and tear" on a joint. Cartilage is the firm, rubbery tissue that cushions the bones at the joints, and allows bones to glide over one another. If the cartilage breaks down and wears away, the bones rub together. This causes pain, swelling, and stiffness. Bony spurs or extra bone may form around the joint. The ligaments and muscles around the joint become weaker and stiffer.

OA symptoms usually appear in middle age. Almost everyone has some symptoms by age 70. However, these symptoms may be minor. Before age 55, OA occurs equally in men and women. After age 55, it is more common in women.[21]

OA tends to run in families. Being overweight increases the risk of OA in the hip, knee, ankle, and foot joints because extra weight causes more wear and tear. Fractures or other joint injuries can lead to OA later in life. This includes injuries to the cartilage and ligaments in joints. Jobs involving kneeling or squatting for more than an hour a day have the highest risk of the development of OA. Jobs that involve lifting, climbing stairs, or walking increase the risk of this disease. Playing sports that involve direct impact on the joint (such as football), twisting (such as basketball or soccer), or throwing also increase the risk of OA.

Medical conditions such as hemophilia can also lead to OA because of bleeding in the joint. Disorders that block the blood supply near a joint lead to avascular necrosis. Other types of arthritis, such as chronic gout, pseudogout, or rheumatoid arthritis lead to "secondary" OA. Systemic diseases also are associated with the development of secondary OA, such as Wilson's disease and hemochromatosis. Hemochromatosis may cause chondrocalcinosis with secondary OA in many joints, especially with a predilection for the second and third metacarpophalangeal joints. OA of non-weight-bearing joints is almost always the result of secondary OA with the exception of some hand joints.

Classification of Osteoarthritis

Primary or idiopathic OA is divided into localized or generalized forms of the disease. Localized OA most commonly affects the hands, feet, knees, hips, and spine. Generalized OA consists of involvement of three or more joint sites. In secondary OA, specific conditions may cause or enhance the risk of developing OA as mentioned above. Secondary OA may also result from trauma, congenital or developmental disorders, septic arthritis, Paget disease of bone, and other diseases such as diabetes mellitus, acromegaly, hypothyroidism, or neuropathic (Charcot) arthropathy.

Clinical Manifestations

Spine. The cervical and lumbar spine is commonly affected. Spinal involvement in OA is most common at C5, T8, and L3, which represent the areas of greatest spinal flexibility. Two

syndromes of clinical importance are due to OA of the lumbar apophyseal joints.[22] In the cervical spine, osteophytes arising from the margins of a vertebral body (cervical spondylosis) may compromise the spinal canal. When sufficiently advanced, cervical spinal cord compression may result. Uncovertebral osteophytes can compromise the neural foramen and impinge on the exiting nerve root. Lumbar apophyseal osteophytes (lumbar spondylosis) can cause spinal stenosis if they encroach into the intervertebral foramina and/or the spinal canal. The resultant symptoms of low back pain radiating to the lower extremity worsens with exertion, thereby mimicking vascular claudication, but resolves more rapidly with rest. Spondylolisthesis, a slipping of one vertebral body on another, typically affecting the apophyseal joints at L4 to L5, may occur with severe OA. Diffuse idiopathic skeletal hyperostosis (DISH) is a syndrome of inappropriate bone formation at the insertions and along the course of ligaments and tendons. Although osteoarthritis is frequently present in patients with the DISH syndrome, the latter is thought to represent a distinct clinical entity.

Hands: Osteoarthritic enlargements of the distal and proximal interphalangeal joints are referred to as Heberden's and Bouchard's node, respectively. The first carpometacarpal joint is also a common area affected by OA. Enlargement of this joint causes a squared appearance to the hand.

Hip: Pain around the hip is common in patients with OA. It may be due to OA of the hip or to pain referred to the hip area from other structures, such as the lumbosacral spine. Similarly, OA of the hip may result in pain that is referred to distant structures (such as the knee).[22] Another potential diagnostic problem is that patients frequently confuse the pain of greater trochanteric bursitis with OA of the hip. The pain from bursitis is felt laterally and does not limit motion; by comparison, OA of the hip is associated with pain in the groin and upper posterior buttock with limited range of motion.

Knee: Osteophytes, effusions, crepitus, and limitation of range of motion are all common signs of OA of the knee. However, findings on physical examination alone may underestimate the degree of knee involvement. In advanced cases, malalignment may be apparent (genu varus or genu valgus), particularly when medial and lateral compartments are affected unequally. Cartilage loss due to OA usually begins in the medial aspect of the tibiofemoral joint; as a result, varus angulation ("bow-legged") occurs more commonly than valgus ("knock-kneed"). Femorotibial malalignment may be a risk factor for more rapid progression of OA of the knee. A fluctuant swelling along the posterior aspect of the knee, or popliteal (Baker's) cyst, is a common complication. Involvement of the patellofemoral portions of the joint may be affected by malalignment.[22]

Feet: The first metatarsophalangeal joint often is affected by OA, resulting in hallux valgus or hallux rigidus. Involvement of the subtalar joint may be particularly troublesome during ambulation; pain is often elicited by inversion and eversion of the foot.[22]

Uncommonly Affected Joints: Shoulder OA is almost always secondary OA. Symptoms of a diseased glenohumeral joint typically include anterior shoulder pain that gradually worsens over years and that is aggravated by movement. Involvement of the acromioclavicular joint may cause vague shoulder pain, which may present a diagnostic dilemma. Osteophytes located along the undersurface of the acromioclavicular joint may result in rotator cuff tendinitis or tears due to the juxtaposition of tendons with the inferior portion of the acromioclavicular joint. The shoulder may rapidly deteriorate because of an aggressive form of OA that occurs in association with calcium crystalline disease.[22] The wrist and elbow may also be affected.

Symptoms

Pain is the principal symptom associated with OA, typically exacerbated by activity and relieved by rest. With more advanced disease, pain may be felt with progressively less activity, eventually occurring at rest and at night. Episodic increases in pain and inflammation suggest synovitis caused by crystalline disease or trauma. Some patients ascribe fluctuating symptoms to changes in the weather, but the evidence for effects of varying barometric pressure, precipitation, and outdoor temperature is conflicting. Pain in OA is not caused directly by cartilage damage since cartilage is aneural. As a result, osteoarthritic radiologic changes are often incidentally noted in patients without symptoms at affected sites. Two general types of pain stimuli in synovial joints can be distinguished: mechanical stimuli, generated by mechanical changes in the environment of the joint (i.e., by direct trauma) and chemical stimuli resulting from tissue inflammation. Stiffness is also a common complaint in patients with OA. Morning stiffness typically resolves in less than 30 minutes after a patient awakens, but may recur following periods of inactivity.

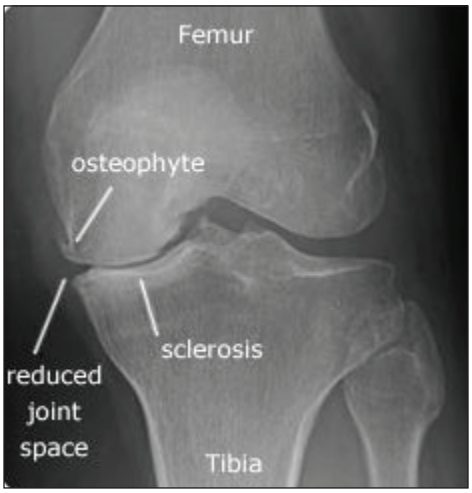
Findings on Physical Examination

Crepitus is a common finding and is probably due to the disruption of the normally smooth articulating surfaces of the joints. Bony enlargement and osteophytes may be palpable as nodules along the periphery of the joint. Tenderness to palpation of involved joints may be evident with or, more often, without associated signs of inflammation. There may also be decreased range of motion and joint malalignment.

Differential Diagnosis:

- Calcium pyrophosphate crystal deposition disease (CPPD disease) — Osteoarthritis of non-weight-bearing joints except the distal interphalangeal joint and proximal interphalangeal joints of the hands is most frequently CPPD disease. Involvement of the second and third metacarpophalangeal (MCP) joints of the hands with OA and the presence of chondrocalcinosis on X-rays of especially knees, the triangular cartilage of the wrist, hips, shoulders, symphasis pubis, and MCPs is frequently due to CPPD disease.
- Rheumatoid arthritis — Unlike OA, rheumatoid arthritis is primarily an inflammatory joint disease with symmetrical joint involvement, and X-ray findings of marginal erosions of joints and

Figure 1. Radiograph of the Knee Demonstrating Features of Osteoarthritis



juxta-articular osteoporosis. It is a systemic disease involving more organ systems than just joints.

- Infectious monoarticular disease — if only one joint is inflamed, arthrocentesis should be performed to rule out infection.
- Most other forms of arthritis — can end up with OA as the final common pathway for joint damage.

Diagnosis: An essential component to the diagnosis is the correct attribution of signs and symptoms to the affected site. As an example, pain and other symptoms resulting from OA can be confused with soft tissue processes such as bursitis at periarticular sites. Additionally, pain in a particular area may be referred from OA at other sites or may be due to a nonarticular process.

Joint pain is a nonspecific symptom, resulting from many possibilities. The physical examination should evaluate the symptomatic joint and adjacent structures. Imaging, as discussed below, is not always necessary. In selected patients, laboratory tests looking for an alternative diagnosis may be useful: serology for rheumatic arthritis and other rheumatologic disease, serum uric acid for gout, and analysis of joint fluid for infection or crystal-induced arthritis.

Certain clinical features are more suggestive of idiopathic OA than other disorders. As an example, OA does not affect all joints equally; it has a predilection for the fingers, knees, hips, and spine, and rarely affects the elbow, wrist, and ankle. If the atypical joints are involved in a patient suspected of having OA, the clinician should initiate a search for secondary causes of the disorder. The joints are usually asymmetrically involved in OA (particularly the large joints), and a synovial effusion, if present, most commonly has mild inflammatory characteristics (i.e., synovial WBC < 2000/mm^3).

Imaging: Imaging can assist by refuting other diagnoses when the clinical picture from history and physical examination leaves this diagnosis unclear.[23] However, the diagnosis is a clinical one made by assessing the constellation of presenting clinical features. Plain radiographs are helpful in assessing for the presence and severity of OA. Radiographic changes in OA are insensitive, particularly with early disease, and correlate poorly with symptoms. When present, however, the specificity of the radiographic changes of OA often renders further diagnostic imaging unnecessary. The major radiographic features of OA include (*see Figure 1*):

- Joint space narrowing;
- Subchondral sclerosis;
- Osteophytes;
- Subchondral cysts.

The clinical relevance of each radiographic finding in OA appears to vary by joint. Minimal joint space of the hip is most closely correlated with hip pain, while osteophytes arising from the patellofemoral and tibiofemoral joints of the knee correlate best with knee pain. Knee joint space narrowing best predicts disease progression.

Magnetic Resonance Imaging (MRI): MRI is not necessary for most patients with suggestive symptoms of OA and/or typical plain radiographic features. However, MRI of the knee has a diagnostic role in patients with joint pain and symptoms such as locking, popping, or instability that suggest meniscal or ligamentous damage. MRI can facilitate the diagnosis of other causes of knee pain that can be confused with osteoarthritis (e.g., osteochondritis dissecans, avascular necrosis, etc.). The presence of a meniscal tear viewed by MRI in a person with knee osteoarthritis is not necessarily a cause of increased symptoms.[23] The presence of two MRI findings concomitantly correlates with painful OA of the knee; partial or full-thickness cartilage defects, and bone marrow "edema" as indicated by decreased T1 and increased T2 signal from the subchondral bone. In contrast, marrow edema alone does not appear to be closely associated with knee pain in patients with generalized osteoarthritis.

Management of Osteoarthritis

The management goals for patients with osteoarthritis include patient education about the disease and its therapy, pain control, improving function, and decreasing disability. Optimal management of OA requires a combination of nonpharmacological and pharmacological modalities.

Nonpharmacologic Therapy

Nonpharmacologic therapies for OA of the knee for which there is reasonably strong evidence of efficacy include exercise programs, weight loss, and patient education. Nonpharmacologic interventions are generally begun before medications.

Lifestyle Changes:

1. Exercise. A pivotal and frequently ignored aspect of conservative treatment of OA is exercise.[24-26] Exercise increases aerobic capacity, muscle strength, and endurance, and also facilitates weight loss.[27,28] All individuals capable of exercise should be encouraged to partake in a low-impact aerobic exercise program (walking, biking, swimming, or other aquatic exercise). Quadriceps strengthening exercises lead to improvements in knee pain and function.[29-31] Guidelines routinely advocate exercise;[21,32-36] however, clinical practice does not often reflect this recommendation.[24-26]

Staying active and getting exercise help maintain joint and overall movement. Water exercises, such as swimming, are especially helpful. Low load effect exercise, warm-up and stretching prior to exercise, and use of splints for joint immobilization can be of benefit for joint protection and reduction in symptoms. All exercise programs include range of motion and isometric strengthening.

2. Other Lifestyle Recommendations: Obesity management and weight loss if overweight are extremely important. The majority of patients with OA are either overweight or obese. There is good evidence for the efficacy of weight management,[27] which is advocated by most OA guidelines. However, in practice, weight management is not frequently implemented.[24-26] In patients with OA who are overweight, weight loss of even modest degree may produce improvement in lower extremity joint pain and function. Other methods of unloading an osteoarthritic joint include canes and walkers, which can reduce joint forces at the hip by as much as 50%. A trial of soft, elastic heeled sports shoes or the use of insoles for patients with knee OA diminishes impact loading.

Moist, superficial heat can raise the threshold for pain, produce analgesia by acting on free nerve endings and decrease muscle spasm.[37-39] Ultrasound therapy appears to have no proven benefit in treating OA. Superficial cooling decreases muscle spasm and increases the threshold of pain. Data concerning the efficacy of transcutaneous electrical nerve stimulation (TENS) in patients with OA are conflicting.[40-42]

Eating a healthy, balanced diet is important. Vitamin D supplementation is indicated in patients at high risk for osteoporosis, such as postmenopausal women. Resting affected joints may alleviate pain. Rest is recommended for only short periods of time, typically 12-24 hours for acute pain and inflammation, because prolonged rest may lead to muscle atrophy and decreased joint mobility. Protecting joints may include the use of braces and splints for symptomatic relief for OA of certain joints such as the knee[43] and OA of the carpometacarpal and interphalangeal joints of the thumb.[44]

Physical Therapy:

Physical therapy can help improve muscle strength and the motion of stiff joints, as well as sense of balance. Therapists have many techniques for treating OA. Physical therapy and exercise improve functional outcome and pain in OA by improving flexibility and by strengthening muscles that support the affected joints.[45] An appropriate exercise program can safely reverse deficiencies in gait, strength, flexibility, aerobic power, and exercise capacity.

Pharmacologic Therapy

Pain is the most salient clinical feature of OA and has the biggest impact on both the welfare and performance of patients. Pain management is therefore of great importance when managing osteoarthritis. However, it should be realized that treatment aimed at pain reduction does not necessarily treat the underlying primary disease process and may even interfere negatively with it. In fact, it has been suggested that long-term use of nonsteroidal anti-inflammatory drugs might enhance the pathologic process of cartilage degeneration by removing the regulatory role of PGE2 on IL-1 synthesis.[46] On the other hand, treatment aimed primarily at pain relief may, through anti-inflammatory actions, also positively affect the articular cartilage by means of inhibition of release of catabolic factors.[47]

Systemic Treatment of Joint Pain:

There are, at present, no specific pharmacologic therapies that can prevent the progression of joint damage due to OA.

Analgesics: Pain relief is the primary indication for the use of pharmacologic agents in patients with OA who do not respond to nonpharmacologic interventions. In patients with noninflammatory OA, this goal is generally achieved by the administration of a non-opioid, simple analgesic.

Acetaminophen: At doses of up to 3 g/day, acetaminophen is the drug of choice for pain relief in this setting.[48,49] Clinical trials found that acetaminophen is superior to placebo, but less effective in relieving pain due to OA of the hip or knee than nonsteroidal anti-inflammatory drugs (NSAIDs).[50] Adverse effects of therapeutic doses of acetaminophen are seldom seen. Hepatotoxicity can occur but, at these doses, is primarily seen only in patients who concurrently consume excessive amounts of alcohol. Acetaminophen in doses of 2 g/day or greater can increase the risk for gastrointestinal (GI) complications, including bleeding and perforation, but these complications are not increased at lower acetaminophen doses. Additionally, the risk of GI complications is greater with the combination of acetaminophen and an NSAID than with either alone.[51] There is suggestive but not definitive evidence that chronic, especially daily, acetaminophen use has dose-dependent, long-term nephrotoxicity.[21]

Tramadol: Tramadol alone or in combination with acetaminophen may also be useful when added to ongoing treatment with an NSAID or COX-2 inhibitor.[52]

Opioid analgesics: Opioid analgesics may be beneficial for short-term use in patients with acute exacerbations of pain. Arguments have also been made for the use of opioids in patients who are not candidates for surgery and who continue to have moderate to severe pain despite being administered NSAIDs or selective cyclooxygenase (COX-2) inhibitors.[53] Opioids may also be considered for patients who are at high risk for adverse effects of both selective COX-2 inhibitors and nonselective nonsteroidal anti-inflammatory drugs (NSAIDs).[49,54]

NSAIDs: NSAIDs are by far the most important class of compounds in this category. NSAIDs may be indicated in patients with noninflammatory OA who fail to respond to acetaminophen or for those with moderate to severe pain. The majority of experience is with oral administration of NSAIDs, although topical preparations are available as well. NSAIDs should be given prior to oral analgesics in patients with inflammatory OA who do not respond to nonpharmacologic interventions.

Oral NSAIDs: NSAIDs are effective pain relievers in OA patients.[55] Many different NSAIDs can be used in patients with symptomatic OA, including over-the-counter agents (aspirin, ibuprofen, and naproxen) and prescription drugs. (*See Table 1.*) There is immense variability in patients' responses to the different agents in terms of both efficacy and toxicity.[56]

- Low dose ibuprofen (< 1600 mg/day) may have less serious gastrointestinal side effects.[57]
- Nonacetylated salicylates (salsalate, choline magnesium trisalicylate), sulindac, and perhaps nabumetone appear to have less renal toxicity.
- The nonacetylated salicylates and

Table 1. Oral NSAIDs

Class	Agent*	Elimination Half-life*	COX-2 Selectivity	Low Dose	Medium Dose	High Dose
Salicylates	Aspirin	0.25 h (as aspirin) 2-6 h (as salicylate)	Non-selective	650 mg QID	650 mg q4h	900 mg q4h
	Diflunisal	8-12 h	Non-selective	250 mg BID	500 mg BID	500 mg TID
	Salsalate	1 h (as salsalate) 4-16 h (as salicylate)	Non-selective	500-750 mg BID	750 mg TID	1000 mg TID
Propionic Acids	Fenoprofen	3 h	Non-selective	200-300 mg QID	600 mg TID-QID	800 mg QID
	Flurbiprofen	6 h	Non-selective	50 mg BID	50 mg TID-QID	100 mg TID
	Ibuprofen	2 h	Non-selective	400 mg TID	600 mg TID-QID	800 mg QID
	Ketoprofen	2 h	Non-selective	25-50 mg TID	75 mg TID	100 mg TID
	Naproxen	12-17 h	Non-selective	250 mg TID	500 mg BID	1250 mg/day divided
	Oxaprozin	22 h	Non-selective	600 mg daily	1200 mg daily	1200 mg daily
Acetic Acids	Diclofenac potassium	2 h	Non-selective	50 mg BID	50 mg TID	50 mg QID
	Diclofenac sodium	2 h	Non-selective	50 mg BID	75 mg BID	50 mg QID§
	Etodolac	6 h	Partially selective	200 mg TID	400 mg BID	1200 mg/day divided
	Indomethacin	5 h	Non-selective	25 mg BID-TID	50 mg BID	50 mg QID
	Sulindac	8 h	Non-selective	150 mg BID	200 mg BID	200 mg BID
Oxicams	Meloxicam	15-20 h	Partially selective	7.5 mg daily	7.5 mg daily	15 mg daily
	Piroxicam	50 h	Non-selective	10 mg daily	20 mg daily	40 mg daily§
Alkanones	Nabumetone	24 h	Partially selective	1000 mg daily	1000 mg BID	1000 mg BID
Coxibs	Celecoxib	11 h	Selective	200 mg daily	200 mg BID	200 mg BID

* Standard (immediate) release preparations
§ Not approved for OA at this dose

nabumetone have less antiplatelet activity.[58]

- Indomethacin should probably be avoided for long-term use in patients with hip OA since it may be associated with accelerated joint destruction in this setting.[59]
- Patients at increased risk of gastroduodenal damage who are receiving low-dose aspirin and a COX-2 selective agent may benefit from anti-ulcer prophylaxis.

Topical NSAIDs: The topical application of NSAIDs may reduce the risk of side effects that are seen with oral use. Topical NSAIDs, such as aspirin and diclofenac, are available as well.

COX-2 Inhibitors: These drugs have at least a 200- to 300-fold selectivity for inhibition of COX-2 over COX-1. However, two selective COX-2 inhibitors, rofecoxib and valdecoxib, were withdrawn from the worldwide market because of an increased risk of serious cardiovascular adverse events associated with their use. Increased cardiovascular risks preclude use of COX-2 selective agents unless the GI risk is very high and the cardiovascular risk is low (e.g., there are no known cardiovascular disease and absence of multiple cardiovascular risk factors). An alternative approach is the use of a nonselective NSAID and a gastroprotective agent such as a proton pump inhibitor or misoprostol. NSAIDs should not be used in combination because of the greater risk of adverse events and the lack of evidence that the use of two or more NSAIDs is associated with improved efficacy. NSAIDs should be avoided in patients with aspirin sensitivity. The selective COX-2 inhibitor, celecoxib, may be less likely to provoke symptoms in aspirin-sensitive reactive airways disease.[48]

Choice of NSAID: There is no convincing evidence that any of the available NSAIDs is more effective than any other for osteoarthritis of the knee or hip.[60,61] Thus, the choice of an NSAID is based upon a variety of other factors including adverse effect profile, cost, type of OA, and frequency of dosage. It is preferable to use an NSAID on a periodic basis in patients with non-inflammatory OA since the presence and intensity of symptoms usually vary with time. A short-acting agent is ideal in this setting.[48] Continuous therapy is indicated if this regimen does not provide adequate symptom control. Because of the pathophysiology, continuous NSAID therapy works better in patients with inflammatory osteoarthritis.

Factors to be considered when

selecting from the available NSAIDs and COX-2 selective agents:

- When NSAID use is considered, the patient should be informed of the potential cardiovascular risk.
- If there is a history of gastroduodenal disease, a selective COX-2 inhibitor may be considered in patients at low cardiovascular risk or a nonselective NSAID can be combined with anti-ulcer prophylaxis.
- A short-acting NSAID is generally used initially. It usually takes about 2-4 weeks to evaluate the efficacy of an NSAID.[56]
- If there is inadequate control with the initial dose, then the dose should be gradually increased toward the maximum for that drug. The patient's renal, liver, and bone marrow function should be monitored as the dose is increased. The patient should be educated to monitor for symptoms indicative of side effects.
- If one NSAID is not effective after 2-4 weeks on a maximal dosage, then another NSAID or nonacetylated salicylate could be tried.

Intraarticular Glucocorticoid Injections: Glucocorticoids inhibit inflammatory mediator production by inhibiting phospholipase A2 through the production of anti-phospholipase proteins called lipocortins.[62] Because of their mode of action upstream in the arachidonic acid cascade, glucocorticoids not only inhibit COX-1/2 derived mediators (including prostaglandins, thromboxanes, and lipoxins), but also the LOX-derived mediators like leukotrienes. Glucocorticoids are primarily potent anti-inflammatory agents, exerting their analgesic action indirectly via the suppression of inflammation. Intraarticular glucocorticoid injections may be appropriate in patients with OA who have one or a few joints that are painful despite the use of an NSAID, and in patients with monoarticular or pauciarticular inflammatory osteoarthritis in whom NSAIDs are contraindicated.[63]

Intraarticular glucocorticoid injections are effective for short-term pain relief and can increase quadriceps strength after knee injection.[64] Glucocorticoids formulated for intraarticular injection are in crystalline suspension. Steroid crystals rarely may lead to a transient mild flare of synovitis. Common synthetic glucocorticoid suspensions used for intraarticular injection include triamcinolone acetonide, triamcinolone hexacetonide, and microcrystalline methylprednisolone. The amount of these agents generally used depends upon joint size:

- 10 mg for small joints (interphalangeal, metacarpophalangeal, and metatarsophalangeal joints)
- 20 mg for medium-sized joints (wrists, elbows, ankles, and acromioclavicular joints)
- 40 mg for larger joints (shoulders, knees, hips).

Intraarticular Hyaluronans: Hyaluronic acid (HA), also called hyaluronan, is a large unsulphated glycosaminoglycan that consists of repeating units of D-gluronic acid and N-acetylglucosamine. Although HA is supposed to treat the primary disease process, not to provide analgesia, as is the case with corticosteroids or NSAIDs, it reportedly also has some analgesic effect itself.[65] In humans, there are various reports on the analgesic effects of HA in OA, but publication bias and flaws in experimental design may have overestimated the beneficial effects in many studies. A meta-analysis showed only a relatively small positive effect of HA application compared with placebo.[66]

There may be subpopulations of patients with osteoarthritis that respond well to this type of therapy. Commercial hyaluronan preparations currently are available in the United States include sodium hyaluronate.

Glucosamine and Chondroitin: The use of glucosamine and chondroitin for OA has been controversial, and results of randomized trials have varied.[67-81] The balance of evidence from high-quality trials has shown little to no evidence of clinically meaningful benefit.[67-69]

Colchicine: The basis for the use of colchicine in inflammatory OA that is refractory to NSAIDs and/or intraarticular glucocorticoids is that the majority of such patients have evidence of calcium pyrophosphate dihydrate crystals.[82] Inflammation is attenuated by colchicine via microcrystal-induced tyrosine phosphorylation.[83] Adding colchicine to ongoing NSAID therapy may produce an additional benefit. This was illustrated in a small study in which 36 patients with OA of the knee were randomly assigned to receive nimesulide plus colchicine (0.5 mg twice daily) or nimesulide plus placebo.[84] Significantly more patients receiving the NSAID plus colchicine combination had at least 30% improvement in osteoarthritis scores (57.9% vs 23.5%, respectively). In view of these findings, it may be reasonable to use prophylactic colchicine (0.6 mg twice daily) in patients with OA if the patient has frequent acute inflammatory episodes that do not respond well to NSAIDs, intraarticular steroid injections, and/or joint irrigation. Chronic colchicine therapy is generally safe in patients who do not have underlying hepatic or renal disease.

Surgery

Severe cases of OA often need surgery to replace or repair damaged joints. The typical indications for surgery are debilitating pain and major limitation of functions, such as walking, working, or sleeping not controlled by other means.[85]

Surgical options include:

- Arthroscopic surgery to trim torn and damaged cartilage, the most common orthopedic surgery performed on the knee, has no demonstrable efficacy.[86]
- Changing the alignment of a bone to relieve stress on the bone or joint (osteotomy)
- Surgical fusion of bones, usually in the spine (arthrodesis)
- Total or partial replacement of the damaged joint with an artificial knee, hip, shoulder, first carpometacarpal, ankle, or elbow joint are regularly done. Currently, the most common indication for knee and hip replacement is OA (approximately 85% of all cases). The general consensus among orthopedic surgeons on indications for joint replacement were (1) severe daily pain and (2) radiographic evidence of joint space narrowing.[85] With proper patient selection, good to excellent

results can be expected in 95% of patients. The survival rate of the implant is expected to be 95% at 15 years.[87] When overall health improvement is used to assess the cost effectiveness of total joint arthroplasty, the hip and knee arthroplasty have similar excellent results.[88]

Prognosis

The prognosis seems to differ according to the affected joint:[89]

- **Hand OA:** Older age appears to be the strongest risk factor for progression.
- **Hip OA:** Risk factors for progression to total hip replacement include female gender, night pain, and lower baseline functional capacity.
- **Knee OA:** A higher body mass index and polyarticular arthritis predict radiographic deterioration. Varus or valgus deformity of the knee correlates with later radiographic worsening of OA of the medial and lateral compartments, respectively.[90,91]

Patients with OA also experience varying degrees of physical disability, and OA can adversely affect quality of life.[92,93] Worsening disability may be correlated with coping styles; in particular, avoidance of activity due to pain may lead to muscle weakness that may impact upon joint stability. Exercise may help to prevent such loss of strength and decrease disability.[94] Joint laxity, impaired proprioception, greater body mass index, and more severe joint pain were each predictive of subsequent worsening in function in patients with OA of the knee.

Mortality

There are some studies showing OA associated with excess mortality risk, although the exact cause could not be determined.[95,96] Risk factors for death included a history of diabetes, cancer, or cardiovascular disease, and the presence of walking disability.

Summary

Several papers document widespread support for OA guidelines, but there are delays in utilization of these standards, particularly of non-pharmacological recommendations, and variance in the application of recommendations by clinicians in different specialty areas.[97-101]

Although the evidence for many OA treatments is good, the complexity and high number of treatment recommendations available for OA may be a hindrance to use of the guidelines.

References

1. Brandt KD, et al. Etiopathogenesis of osteoarthritis. *Med Clin North Am* 2009;93:1-24.
2. Covinsky K. Aging, arthritis, and disability. *Arthritis Rheum* 2006;55:175-176.
3. Covinsky KE, et al. Effect of arthritis in middle age on older-age functioning. *J Am Geriatr Soc* 2008;56:23-28.
4. Dunlop D, et al. Disability in activities of daily living: Patterns of change and a hierarchy of disability. *Am J Public Health* 1997;87:378-383.
5. Dunlop D, et al. Arthritis prevalence and activity limitations in older adults. *Arthritis Rheum* 2001;44:212-221.
6. Felson D, et al. Osteoarthritis: New insights. Part 1: The disease and its risk factors [review]. *Ann Intern Med* 2000;133:635-646.
7. Institute of Medicine. *The Future of Disability in America*. Washington, DC: The National Academies Press; 2007.
8. Ling SM, et al. Transitions to mobility difficulty associated with lower extremity osteoarthritis in high functioning older women: Longitudinal data from the Women's Health and Aging Study II. *Arthritis Rheum* 2006;55:256-263.
9. Song J, et al. Population impact of arthritis on disability in older adults. *Arthritis Rheum* 2006;55:248-255.
10. Verbrugge LM, Juarez L. Profile of arthritis disability: II. *Arthritis Rheum* 2006;55:102-113.
11. van Saase JL, et al. Epidemiology of arthritis: Zoetermeer survey. Comparison of radiological arthritis in a Dutch population with that of 10 other populations. *Ann Rheum Dis* 1989;20:351-369.
12. Lawrence J, et al. Prevalence in the population and relationships between symptoms and x-ray changes. *Ann Rheum Dis* 1966;25:1-24.
13. Mow VC, et al. Cartilage and diarthrodial joints as paradigms for hierarchical materials and structures. *Biomaterials* 1992;13:67.
14. Mankin HJ, Brandt KD. Biochemistry and metabolism of articular cartilage in osteoarthritis. In: *Osteoarthritis: Diagnosis and Management*, 2nd edition. Moskowitz RW, eds. Philadelphia: WB Saunders; 1992: 109.
15. Byer PD, et al. Hypothesizing about joints. In: *Studies in Joint Diseases 2*. Maroudas A, Holborow EJ, eds. London: Pitman; 1983: 241.
16. Jimenez SA, et al. Type II collagen gene mutations in familial osteoarthritis. In: *Articular Cartilage and Osteoarthritis* (workshop). Kuettner KE, et al, eds. New York: Raven Press; 1992: 167.
17. Mizrahi J, et al. The "instantaneous" deformation of cartilage: Effects of collagen fiber orientation and osmotic stress. *Biorheology* 1986;23:311.
18. Smith MD, et al. Synovial membrane inflammation and cytokine production in patients with early osteoarthritis. *J Rheumatol* 1997;24:365.
19. Fava R, et al. Active and latent forms of transforming growth factor beta activity in synovial effusions. *J Exp Med* 1989;169:291.
20. McAlindon TE, et al. Relation of dietary intake and serum levels of vitamin D to progression of osteoarthritis of the knee among participants in the Framingham Study. *Ann Intern Med* 1996;125:353.
21. Hunter D. In the clinic. Osteoarthritis [review]. *Ann Intern Med* 2007;147. ITC8-1-16.
22. Moskowitz RW, Holderbaum D. Clinical and laboratory findings in osteoarthritis. In: *Arthritis and Allied Conditions*. Koopman WJ, ed. Baltimore: Williams & Wilkins; 2001: 2216.
23. Altman R, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum* 1986;29:1039-1049.
24. DeHaan MN, et al. Knee osteoarthritis clinical practice guidelines — how are we doing? *J Rheumatol* 2007;34:2099-2105.
25. Hutchings A, et al. The Longitudinal Examination of Arthritis Pain (LEAP) study: Relationships between weekly fluctuations in patient-rated joint pain and other health outcomes. *J Rheumatol* 2007;34:2291-2300.
26. Jordan KM, et al. The use of conventional and complementary treatments for knee osteoarthritis in the community. *Rheumatology* 2004;43:381-384.
27. Messier SP, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: The arthritis, diet, and activity promotion trial [see comment]. *Arthritis Rheum* 2004;50: 1501-1510.

28. Ettinger WHJ, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA* 1997;277:25-31.
29. Roddy E, et al. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Ann Rheum Dis* 2005;64:544-548.
30. Roddy E, et al. Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee—the MOVE consensus. *Rheumatology* 2005;44:67-73.
31. Schattner A. Review: Both aerobic and home-based quadriceps strengthening exercises reduce pain and disability in knee osteoarthritis. *ACP J Club* 2005;143:71.
32. Jordan KM, et al. EULAR recommendations 2003: An evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2003;62:1145-1155.
33. Zhang W, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2005;64:669-681.
34. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000;43:1905-1915.
35. Zhang W, et al. OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008;16:137-162.
36. Hunter D, Felson D. Osteoarthritis. *BMJ* 2006;332:639-642.
37. Hollander JL, Horvath SM. The influence of physical therapy procedures on the intra-articular temperature of normal and arthritic subjects. *Am J Med Sci* 1949;218:543.
38. Fischer E, Solomon S. Physiological responses to heat and cold. In: *Therapeutic Heat and Cold*. Licht S, Ed, E Licht, New Haven, CT; 1965:126.
39. Hicks JE, Gerber LH. Rehabilitation in the management of patients with osteoarthritis. In: *Osteoarthritis: Diagnosis and Medical/Surgical Management*, Moskowitz RW, et al. eds. Philadelphia: WB Saunders; 1992:433.
40. Zizic TM, et al. The treatment of osteoarthritis of the knee with pulsed electrical stimulation. *J Rheumatol* 1995;22:1757.
41. Taylor P, et al. Treatment of osteoarthritis of the knee with transcutaneous electrical nerve stimulation. *Pain* 1981;11:233.
42. Lewis B, et al. The comparative analgesic efficacy of transcutaneous electrical nerve stimulation and a non-steroidal anti-inflammatory drug for painful osteoarthritis. *Br J Rheumatol* 1994;33:455.
43. Draper ER, et al. Improvement in function after valgus bracing of the knee. An analysis of gait symmetry. *J Bone Joint Surg Br* 2000;82:1001.
44. Rannou F, et al. Splint for base-of-thumb osteoarthritis: A randomized trial. *Ann Intern Med* 2009;150:661.
45. Fransen M, et al. Physical therapy is effective for patients with osteoarthritis of the knee: A randomized controlled clinical trial. *J Rheumatol* 2001;28:156.
46. Landoni MF, et al. Effects of flunixin, tolfenamic acid, R(-) and S (1) ketoprofen on the response of equine synoviocytes to Lipopolysaccharide stimulation. *Equine Vet J* 1996;28:468-475.
47. De Grauw JC, et al. In vivo effects of meloxicam on inflammatory mediators, MMP activity and cartilage biomarkers in equine joints with acute synovitis. *Equine Vet J* 2009;41:693-699.
48. Hochberg MC, et al. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. American College of Rheumatology. *Arthritis Rheum* 1995;38:1535.
49. Jordan KM, et al. EULAR Recommendations 2003: An evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2003;62:1145.
50. Towheed TE, et al. Acetaminophen for osteoarthritis. *Cochrane Database Syst Rev* 2006;CD004257.
51. Doherty M, et al. A randomised controlled trial of ibuprofen, paracetamol or a combination tablet of ibuprofen/paracetamol in community-derived people with knee pain. *Ann Rheum Dis* 2011;70:1534.
52. Cepeda MS, et al. Tramadol for osteoarthritis. *Cochrane Database Syst Rev* 2006;CD005522.
53. Peloso PM. Opioid therapy for osteoarthritis of the hip and knee: Use it or lose it? *J Rheumatol* 2001;28:6.
54. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000;43:1905.
55. Bjordal JM, et al. Non-steroidal anti-inflammatory drugs, including cyclo- oxygenase-2 inhibitors, in osteoarthritic knee pain: Meta-analysis of randomised placebo controlled trials. *BMJ* 2004;329:1317.
56. Batchlor EE, Paulus HE. Principles of drug therapy. In: *Osteoarthritis: Diagnosis and Medical/Surgical Management*. Moskowitz RW, et al, eds. Philadelphia: WB Saunders Co.; 1992:465.
57. Griffin MR, et al. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. *Ann Intern Med* 1991;114:257.
58. Furst DE. Are there differences among nonsteroidal anti-inflammatory drugs? Comparing acetylated salicylates, nonacetylated salicylates, and nonacetylated nonsteroidal anti-inflammatory drugs. *Arthritis Rheum* 1994;37:1.
59. Huskisson EC, et al. Effects of anti-inflammatory drugs on the progression of osteoarthritis of the knee. LINK Study Group. Longitudinal Investigation of Nonsteroidal Anti-inflammatory Drugs in Knee Osteoarthritis. *J Rheumatol* 1995;22:1941.
60. Watson MC, et al. Non-aspirin, non-steroidal anti-inflammatory drugs for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2000; CD000142.
61. Towheed T, et al. Analgesia and non-aspirin, non-steroidal anti-inflammatory drugs for osteoarthritis of the hip. *Cochrane Database Syst Rev* 2000; CD000517.
62. Di Rosa RJ, et al. Nomenclature announcement. Anti-phospholipase proteins. *Prostaglandins* 1984;28:441-442.
63. Newstadt DH. Intraarticular steroid therapy. In: *Osteoarthritis: Diagnosis and Medical/Surgical Management.* Moskowitz RW, et al., eds. Philadelphia: WB Saunders Co; 1992:493.
64. Arroll B, Goodyear-Smith F. Corticosteroid injections for osteoarthritis of the knee: Meta-analysis. *BMJ* 2004;328:869.
65. Moskowitz RW. Hyaluronic acid supple mentation. *Curr Rheumatol Rep* 2000;2:466-471.
66. Lo GH, et al. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: A meta-analysis. *JAMA* 2003;290:3115-1121.
67. Clegg DO, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006;354:795.
68. Sawitzke AD, et al. Clinical efficacy and safety of glucosamine, chondroitin sulphate, their combination, celecoxib or placebo taken to treat osteoarthritis of

the knee: 2-year results from GAIT. *Ann Rheum Dis* 2010;69:1459.

69. Wandel S, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: Network meta-analysis. *BMJ* 2010;341:c4675.
70. Setnikar I, et al. Antiarthritic effects of glucosamine sulfate studied in animal models. *Arzneimittelforschung* 1991;41:542.
71. Biggee BA, et al. Low levels of human serum glucosamine after ingestion of glucosamine sulphate relative to capability for peripheral effectiveness. *Ann Rheum Dis* 2006;65:222.
72. Towheed TE, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database Syst Rev* 2005; CD002946.
73. Vlad SC, et al. Glucosamine for pain in osteoarthritis: Why do trial results differ? *Arthritis Rheum* 2007;56:2267.
74. Reginster JY. The efficacy of glucosamine sulfate in osteoarthritis: Financial and nonfinancial conflict of interest. *Arthritis Rheum* 2007;56:2105.
75. Reginster JY, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: A randomised, placebo-controlled clinical trial. *Lancet* 2001;357:251.
76. Mazzuca SA, et al. Knee pain reduces joint space width in conventional standing anteroposterior radiographs of osteoarthritic knees. *Arthritis Rheum* 2002;46:1223.
77. Pavelká K, et al. Glucosamine sulfate use and delay of progression of knee osteoarthritis: A 3-year, randomized, placebo-controlled, double-blind study. *Arch Intern Med* 2002;162:2113.
78. Rozendaal RM, et al. Effect of glucosamine sulfate on hip osteoarthritis: A randomized trial. *Ann Intern Med* 2008;148:268.
79. Rozendaal RM, et al. Effect of glucosamine sulphate on joint space narrowing, pain and function in patients with hip osteoarthritis; subgroup analyses of a randomized controlled trial. *Osteoarthritis Cartilage* 2009;17:427.
80. Cibere J, et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum* 2004;51:738.
81. Reichenbach S, et al. Meta-analysis: Chondroitin for osteoarthritis of the knee or hip. *Ann Intern Med* 2007;146:580.
82. Klashman DJ, et al. Occult presence of CPPD crystals in patients undergoing arthroscopic knee irrigation for refractory pain related to osteoarthritis (abstract). *Arthritis Rheum* 1994;37:S240.
83. Roberge CJ, et al. Crystal-induced neutrophil activation. IV. Specific inhibition of tyrosine phosphorylation by colchicine. *J Clin Invest* 1993;92:1722.
84. Das SK, et al. A randomized controlled trial to evaluate the slow-acting symptom-modifying effects of colchicine in osteoarthritis of the knee: A preliminary report. *Arthritis Rheum* 2002;47:280.
85. Mancuso CA, et al. Indications for total hip and total knee arthroplasties. Results of orthopaedic surveys. *J Arthroplasty* 1996;11:34-46.
86. Moseley JB, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347:81–88.
87. Callahan CM, et al. Patient outcomes following tricompartmental total knee replacement. A meta-analysis. *JAMA* 1994;271:1349-1357.
88. Ethgen O, et al. Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *J Bone Joint Surg Am* 2004;86:963-974.
89. Hochberg MC. Prognosis of osteoarthritis. *Ann Rheum Dis* 1996;55:685.
90. Cahue S, et al. Varus-valgus alignment in the progression of patellofemoral osteoarthritis. *Arthritis Rheum* 2004;50:2184.
91. Sharma L, et al. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA* 2001;286:188.
92. Dominick KL, et al. Health-related quality of life among older adults with arthritis. *Health Qual Life Outcomes* 2004;2:5.
93. Losina E, et al. Impact of obesity and knee osteoarthritis on morbidity and mortality in older Americans. *Ann Intern Med* 2011;154:217.
94. Steultjens MP, et al. Avoidance of activity and disability in patients with osteoarthritis of the knee: The mediating role of muscle strength. *Arthritis Rheum* 2002;46:1784.
95. van Dijk GM, et al. Course of functional status and pain in osteoarthritis of the hip or knee: A systematic review of the literature. *Arthritis Rheum* 2006;55:779.
96. Hochberg MC. Mortality in osteoarthritis. *Clin Exp Rheumatol* 2008;26:S120.
97. DeHaan MN, et al. Knee osteoarthritis clinical practice guidelines — how are we doing? *J Rheumatol* 2007;34:2099-2105.
98. Jawad AS. Analgesics and osteoarthritis: Are treatment guidelines reflected in clinical practice? *Am J Ther* 2005;12:98-103.
99. Denoeud L, et al. First line treatment of knee osteoarthritis in outpatients in France: Adherence to the EULAR 2000 recommendations and factors influencing adherence. *Ann Rheum Dis* 2005;64:70-74.
100. Mazieres B, et al. Level of acceptability of EULAR recommendations for the management of knee osteoarthritis by practitioners in different European countries. *Ann Rheum Dis* 2005;64:1158-1164.
101. Sarzi-Puttini P, et al. Do physicians treat symptomatic osteoarthritis patients properly? Results of the AMICA experience. *Semin Arthritis Rheum* 2005;35:38-42.

CME Questions

1. What is the leading cause of disability among adults?
   A. smoking
   B. alcohol
   C. osteoarthritis
   D. COPD
2. Osteoblasts play a role in the formation of osteoarthritis.
   A. true
   B. false
3. Which of the following does *not* distinguish pain from OA of the hip from greater trochanteric bursitis?
   A. OA pain radiates to the groin and upper posterior buttock.
   B. Bursitis pain does not limit motion.
   C. OA pain limits motion.
   D. Bursitis pain is felt anteriorly.
4. Which joints of the hand are commonly affected in osteoarthritis?
   A. proximal interphalangeal joints
   B. distal interphalangeal joints
   C. carpometacarpal of the thumb
   D. all of the above
5. What is the main radiographic change seen with osteoarthritis?
   A. joint space narrowing
   B. subchondral sclerosis
   C. osteophytes
   D. subchondral cysts
   E. all of the above
6. Acetaminophen in excess of how many grams per day increases the risk for GI complications?
   A. 1 g/day
   B. 2 g/day
   C. 3 g/day
   D. 4 g/day
7. Compared to non-selective NSAIDs, the selective COX-2 inhibitors have a higher risk for cardiovascular adverse effects.
   A. true
   B. false
8. How long does it usually take to determine the efficacy of an initial

dose of short-acting NSAID in the treatment of OA?
A. one week
B. 2 to 4 weeks
C. 6 to 8 weeks
D. three months

9. Which of the following is *not true* regarding intraarticular glucocorticoid injections in OA?
A. They prevent further joint destruction.
B. They provide short-term pain relief in OA of the knee.
C. They are useful in pauciarticular OA when NSAIDs are contraindicated.
D. They may rarely produce a transient mild flare of synovitis.

10. Glucosamine and chondroitin are effective in OA of the knee.
A. true
B. false

EMERGENCY MEDICINE REPORTS

CME Objectives

Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in patients presenting to the emergency department;
- apply state-of-the-art diagnostic and therapeutic techniques to patients with the particular medical problems discussed in the publication;
- discuss the differential diagnosis of the particular medical problems discussed in the publication;
- explain both the likely and rare complications that may be associated with the particular medical problems discussed in the publication.

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:

1. Read and study the activity, using the references for further research.
2. Scan the QR code to the right or log on to www.cmecity.com, or log on to the new AHCMedia.com and select "MyAHC" then "My Courses."
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After completing the test, your browser will be directed to the activity evaluation form.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

EMERGENCY MEDICINE REPORTS™
(ISSN 0746-2506) is published every other week by AHC Media LLC, One Atlanta Plaza, 950 East Paces Ferry Road NE, Suite 2850, Atlanta, GA 30326. Telephone: (800) 688-2421 or (404) 262-7436.

Editorial & Continuing Education Director: Lee Landenberger

Executive Editor: Shelly Morrow Mark

GST Registration No.: R128870672

Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to ***Emergency Medicine Reports,*** P.O. Box 550669, Atlanta, GA 30355.

Back issues: $31. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

AHC Media

SUBSCRIBER INFORMATION

CUSTOMER SERVICE: 1-800-688-2421

Customer Service E-Mail Address:
customerservice@ahcmedia.com

Editorial E-Mail Address:
shelly.mark@ahcmedia.com

World-Wide Web page:
www.ahcmedia.com

SUBSCRIPTION PRICES

1 year with 65 ACEP/65 AMA/39 AAFP Category 1/Prescribed credits: $564

1 year *without* credit: $419
Add $19.99 for shipping & handling

MULTIPLE COPIES:
Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.

One to nine additional copies:
$359 each;
10 or more additional copies:
$319 each.

All prices U.S. only. U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

ACCREDITATION

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of 65 *AMA PRA Category 1 Credits™*. Each issue has been designated for a maximum of 2.50 *AMA PRA Category 1 Credits™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Approved by the American College of Emergency Physicians for a maximum of 65.00 hour(s) of ACEP Category I credit.

This Enduring Material activity, Emergency Medicine Reports, has been reviewed and is acceptable for up to 39.00 Prescribed credits by the American Academy of Family Physicians. Term of approval begins 01/01/2015. Term of approval is for one year from this date. Each monograph is approved for 1.50 Prescribed credits. Credit may be claimed for one year from the date of each monograph. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic Association has approved this continuing education activity for up to 65 AOA Category 2-B credits.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

This CME activity is intended for emergency and family physicians. It is in effect for 36 months from the date of the publication.