

Knee Pain or Swelling: Acute or Chronic

Knee Pain Guideline Team

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

Patient population: Pediatric and adult.

Objectives: (1) Facilitate a comprehensive, yet efficient evaluation of knee pain. (2) Recommend appropriate use of knee x-rays and MRI. (3) Provide optimal treatment of knee pain. (4) Identify indications for consultation.

Key points

■ Diagnosis

- The majority of knee pain is caused by patellofemoral syndrome and osteoarthritis [evidence: D*].
- MRI of the knee has been proven not to be superior to the clinical exam by an experienced examiner in the evaluation of acute knee injuries [A*]. MRI may be useful to assess bone pathology underlying chronic knee pain [D*].
- Differentiating between knee pain without constitutional symptoms (Figure 1), knee pain with constitutional symptoms (Figure 2), and traumatic knee pain (Figure 3) is helpful in determining a diagnosis.
- Patients with knee pain and swelling who have non-bloody aspirates may also have serious knee pathology (Figure 4).

■ Treatment

- Exercises are important. Many knee conditions will improve with conservative treatment consisting of low impact activities and exercises to improve muscular strength and flexibility. Patellofemoral dysfunction is best treated with vastus medialis strengthening and hamstring and calf stretching [B*].
- In most cases a home treatment program should be explained in detail to the patient, including specific guidelines for activity modification and exercises. Initially, formal physical therapy is usually not required.
- All patients with mild to moderate knee osteoarthritis who do not have medical contraindications should be offered an exercise program that includes lower extremity strengthening and stretching exercises combined with low impact aerobic exercises (e.g., swimming, biking, walking, cross-country skiing) [A*].
- The initial drugs of choice for the treatment of the pain of knee osteoarthritis are acetaminophen and/or topical capsaicin [A*]. If a traditional NSAID is indicated, the choice should be based on cost (see Table 6). COX-2-Inhibitors are no more effective than traditional NSAID agents; they may offer a short-term but probably no long-term advantage in GI tolerance for some patients. Due to cost and increased heart attack risk, COX-2 inhibitors should be reserved for carefully selected patients (see Table 7).

■ Follow-up

- Symptoms should not be allowed to persist for more than 12 weeks before a reevaluation of the condition, along with possible consultation with physical therapy or a musculoskeletal specialist (e.g., orthopedic surgeon, rheumatologist, physiatrist, or sports medicine specialist) [D*].

* Levels of evidence for the most significant recommendations

A = randomized controlled trials; B = controlled trials, no randomization; C = observational trials; D = opinion of expert panel

Clinical Background

Clinical Problem and Clinical Dilemma

Knee pain is a common presenting complaint in primary care. In addition, approximately 1.3 million patients are seen annually in United States emergency departments with the problem of acute

knee trauma. The majority of knee pain is caused by patellofemoral syndrome and osteoarthritis which respond well to knee strengthening exercises and symptomatic care. Plain x-rays and MRI are usually not useful for the evaluation of atraumatic knee pain unless indicated by history and physical examination.

(Continued on page 8)

Figure 2. Knee Pain with Constitutional Symptoms

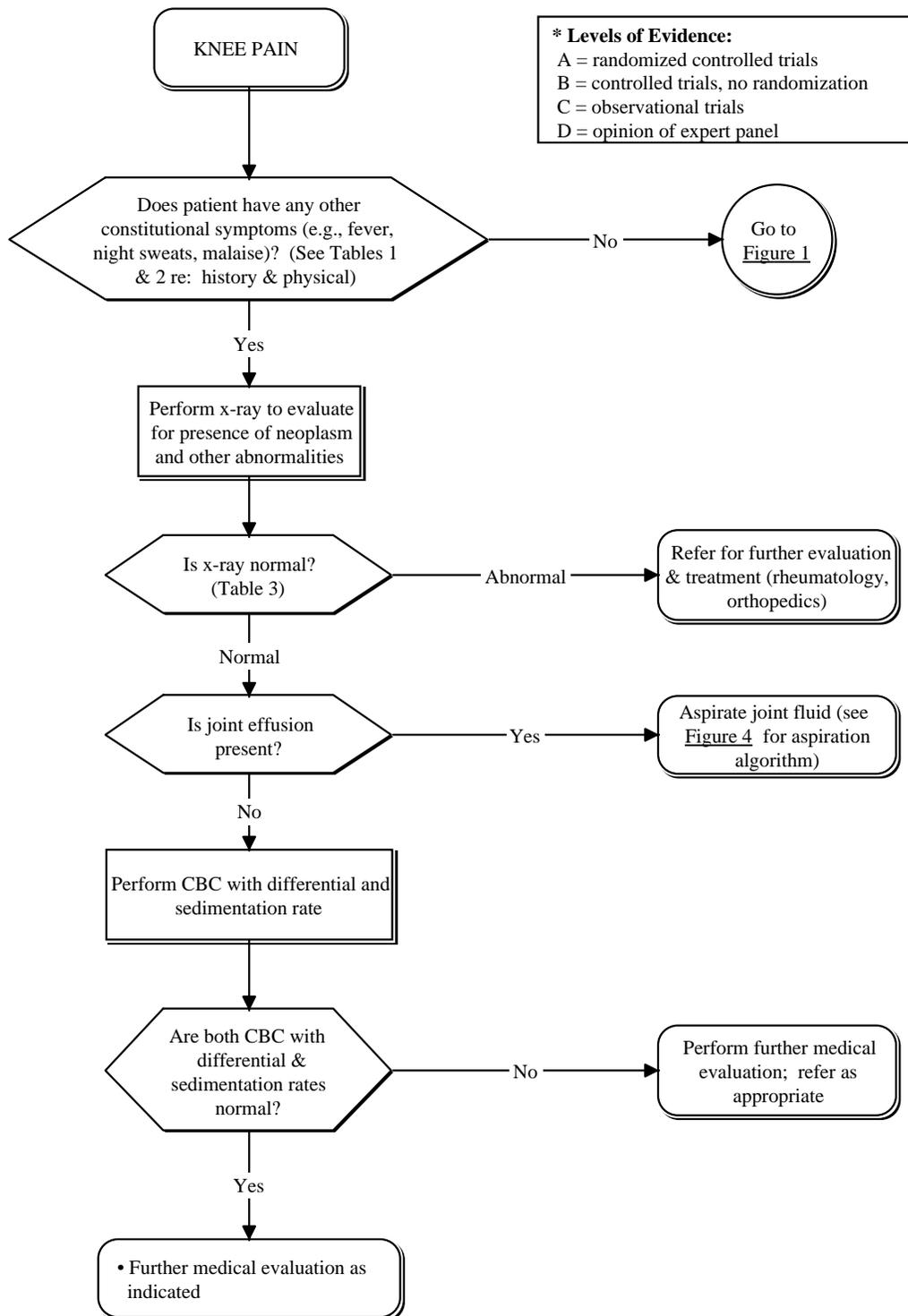


Figure 3. Traumatic Knee Pain

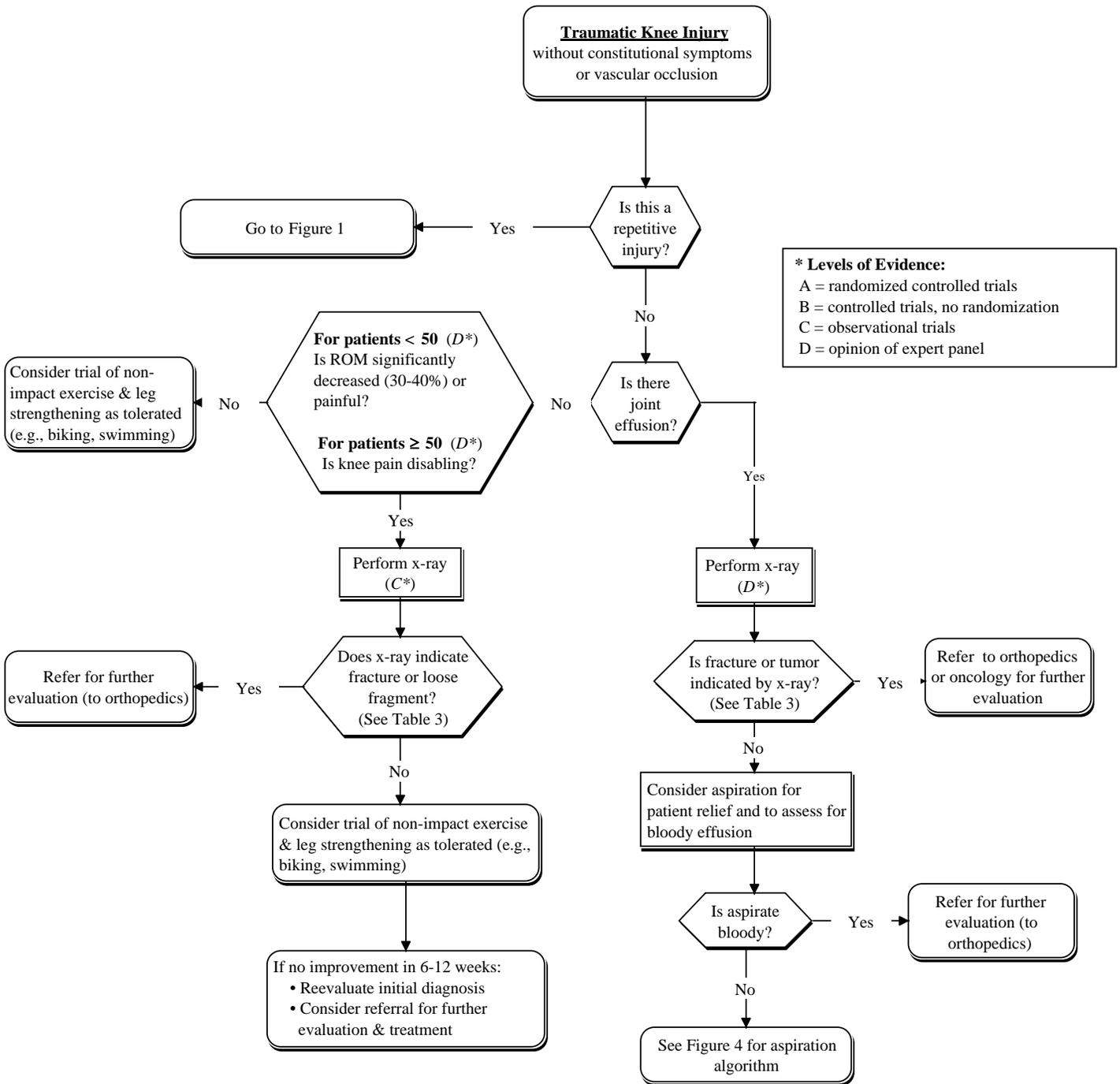


Figure 4. Knee Effusion that is Not Grossly Bloody

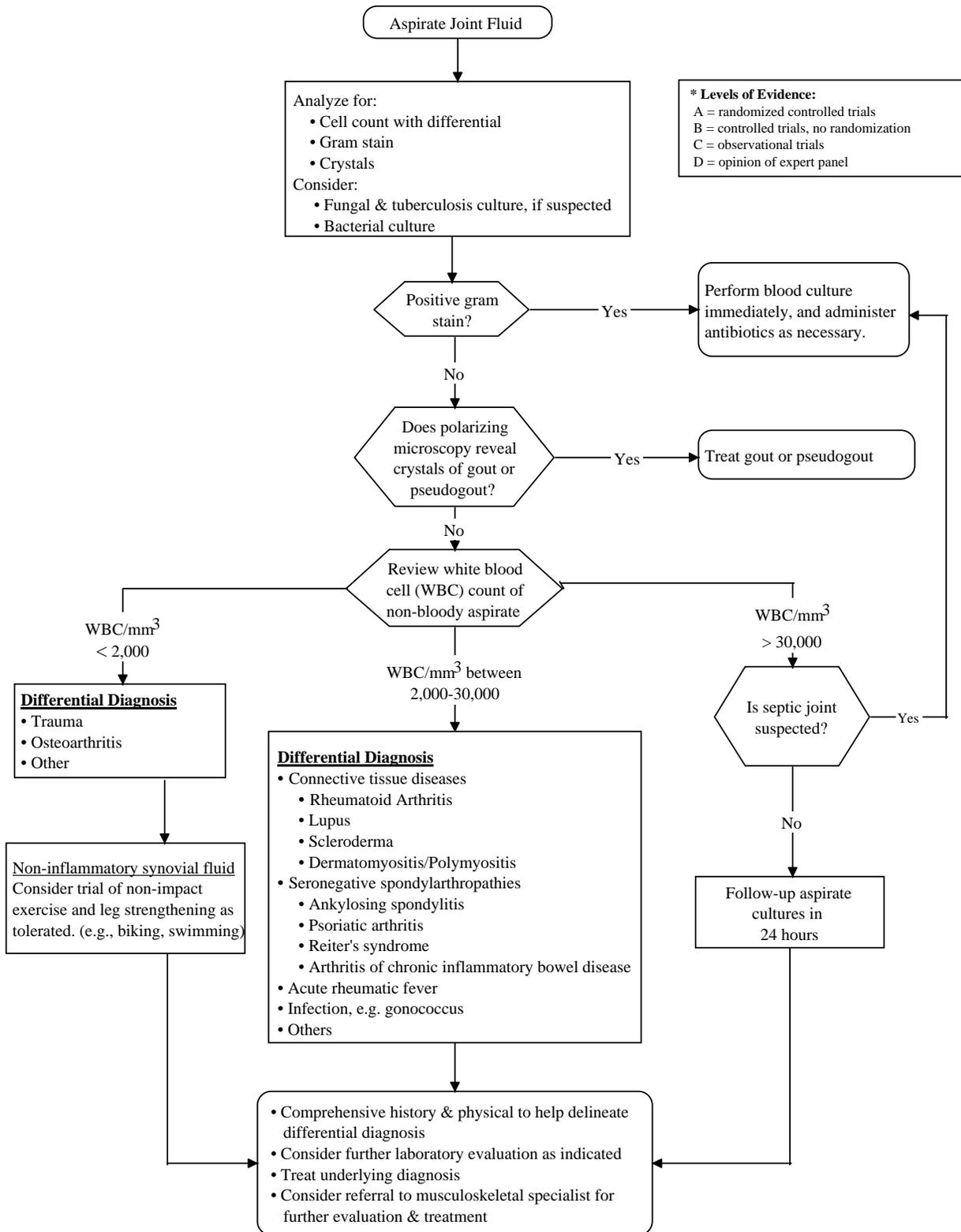


Table 1. Significant History

- Onset, history and location of pain
- Previous history of similar problems in knee or other joints
- Response to activity
- Factors that aggravate pain
- Factors that relieve pain
- Presence and location of swelling
- Stiffness
- Grinding, catching, locking or snapping
- Fever or chills
- Change in sensation or muscle strength

Table 3. Abnormal X-ray Findings

- Neoplasm
- Fracture
- Intraarticular loose body
- Effusion

Table 2. Significant Physical Examination

- Visual inspection for dislocations & fractures
- Presence and location of swelling (intraarticular, prepatellar bursa, posterior)
- Presence and location of warmth
- Presence and location of crepitus
- Foot pulses
- Palpate for tenderness (peripatellar, patella, patella tendon, tibial tuberosity, medial and lateral joint lines, medial and lateral collateral ligaments, and pes anserine bursa)
- Apprehension and pain with lateral displacement of patella for indications of patella subluxation or dislocation
- Active range of motion (normal = 0°-135°)
- Passive range of motion
- Joint line pain with extension or flexion is compatible with meniscus tear
- Meniscal compression tests (McMurray's, Appley's) to evaluate for torn meniscus
- Varus/valgus instability (0° & 30° of flexion) for damage to collateral ligaments
- Evaluate hip range of motion for underlying hip pathology
- Survey other joints for signs of underlying rheumatologic disorder

Table 4. Therapeutic Exercises

- For most conditions, avoid high impact and full weight bearing activities such as jumping, twisting, and running on hard surfaces until injury has healed and patient is pain free.
- Quadriceps strengthening (specifically the vastus medialis obliques by straight leg raises, quad sets, and leg presses as tolerated).
- Hamstring and calf stretching.
- Low impact aerobic activities such as cycling, swimming, walking, cross country skiing.
- For most patients, home exercise programs are as effective as formal physical therapy.
- Consider formal physical therapy for patients who need supervision, or who would benefit from a biomechanical assessment that could be done by a physical therapist.

Table 5. Treatment Modalities

- **Rest, Ice:** 15-20 minutes every 3-4 hours for first 24-48 hours.
- **Crutches:** Should be used if unable to bear full weight without pain or for specific conditions for which non-weight bearing is indicated (e.g., fractures, osteochondritis dessicans). If partial weight bearing is acceptable, encourage range of motion and weight bearing as tolerated.
- **Bracing:** Indicated only if injury is unstable and needs immobilization, or for specific support of an injured structure when the diagnosis has been established (e.g., collateral ligament sprains). Routine use of immobilizers is discouraged because resulting stiffness and pain delays recovery.
- **Non-steroidal anti-inflammatory agents:** Evidence is lacking for impact on outcome of osteoarthritis. May be useful to decrease swelling. Probably the drugs of choice for inflammatory arthritis. Other less toxic agents have been proven to be equally efficacious as analgesics (e.g., acetaminophen, capsaicin cream).
- **Intraarticular injection of anesthetic and corticosteroid:** Best used for unremitting pain from chronic conditions (e.g., degenerative joint disease). Not indicated for acute injuries. Frequency of injections not established, but consensus is that these should not be administered more often than every 3-6 months. Potential side effects include introduction of infection, skin necrosis, tendon and cartilage weakening, and systemic effects of corticosteroids (especially hyperglycemia). It is important to establish diagnosis before administering intraarticular steroids.

Table 6. Pharmacological Therapy for Knee Pain

Generic Name	Brand Name	Usual Adult Dose	Cost for 30 days*		Usual Pediatric Dose	Cost for 30 days - 20 kg child	
			Generic	Brand		Generic	Brand
<u>Acetaminophen</u>							
Acetaminophen	Tylenol	1 gm po qid	\$3	\$19	40 mg/kg divided QID	\$4	\$24
<u>Salicylates</u>							
Aspirin	(various)	325 mg 2 tabs po qid	\$5	\$10	80 – 100 mg/kg div QID*	\$3	\$6
Salsalate	Disalcid	500 mg 2 tabs po tid	\$22	NA	Older only – adult dosing		
Diflunisal	Dolobid	500 mg po bid	\$61	\$80			
Tri Salicylate	Trilisate	3 gm po daily	NA	\$159	30 – 50 mg/kg div QID*	\$25	\$49
<u>Traditional NSAIDs</u>							
Ibuprofen	Nuprin, Motrin, Advil	600 mg po qid	\$9	\$21	40 mg/kg div QID	\$8	\$11
Indomethacin	Indocin	50 mg po tid	\$14	NA	1.5 – 3 mg/kg div TID	NA	\$51
Diclofenac Sodium	Voltaren	75 mg po bid	\$17	\$138	Older only – adult dosing		
	Voltaren-XR	100 mg daily	\$58	\$138	Older only – adult dosing		
Ketoprofen	Orudis	50 mg po qid	\$20	NA	Older only – adult dosing		
	Oruvail	200 mg po daily	\$34	\$92	Older only – adult dosing		
Naproxen	Aleve, Anaprox, Naprosyn, Naprelan	500 mg po bid	\$12	\$103	15 – 20 mg/kg div BID	\$10	\$16
Nabumetone	Relafen	1 gm po daily	\$55	\$96	Older only – adult dosing		
Flurbiprofen	Ansaid	100 mg po tid	\$47	\$202	Older only – adult dosing		
Sulindac	Clinoril	200 mg po bid	\$27	\$81	Older only – adult dosing		
Etodolac	Lodine	1 gm po daily	\$38	\$101	Older only – adult dosing		
Diclofenac potassium	Cataflam	50 mg po tid	\$70	\$236	Older only – adult dosing		
Oxaprozin	Daypro	1200 mg po daily	\$31	\$115	Older only – adult dosing		
Piroxicam	Feldene	20 mg po daily	\$6	\$97	Older only – adult dosing		
Meloxicam	Mobic	15 mg po daily	NA	\$112	Older only – adult dosing		
<u>COX-2 Inhibitors**</u>							
Celecoxib	Celebrex	200 mg po daily	NA	\$84	Older only – adult dosing		
<u>Combination</u>							
Diclofenac Sodium & Misoprostol	Arthrotec 50	1 tab po tid	NA	\$164			
	Arthrotec 75	1 tab po bid	NA	\$110			
<u>Alternative Medicine</u>							
Glucosamine & Chondroitin	Various OTC brands	500 mg / 400 mg – 1 tab tid	\$30 -\$60 (Cost may vary by store or brand – sold OTC)		Older only – adult dosing		
<u>Hyaluronic acid</u>							
Hyaluronate sodium	Hyalgan	single-use syringe		\$143			
Hylan GF-20	Synvisc	single-use syringe		\$224			

* Cost: For brand drugs (average wholesale price-10%) Amerisource Bergen Wholesale Catalog 8/1/04. For generic drugs, Maximum Allowable Cost plus \$3 BCBS MAC List, 6/7/04.

** Recommended daily rather than bid for cost-effectiveness. Avoid in patients with cardiac risk factors.

Table 7. COX-2 Criteria and Precautions

<p>Patient:</p> <ol style="list-style-type: none">1) has a history of upper GI bleeding2) is receiving chronic, high dose systemic corticosteroids3) has presence of a bleeding disorder4) is receiving anticoagulants5) has a documented intolerance to traditional NSAIDs6) elderly patients with multiple comorbidities <p>Note: Do not prescribe COX-2s to patients with known coronary heart disease. Exercise extreme caution in prescribing to patients with multiple risk factors for coronary heart disease (see page 9).</p>

Rationale for Recommendations

Evaluation and Treatment

The history and physical exam are the most important components of the evaluation, and should focus on differentiating the causes of knee pain, which include anterior knee pain (e.g., patellofemoral syndrome), osteoarthritis, bursitis, tendonitis, inflammatory arthritis, and internal derangement (e.g., meniscal or ligament tear). Recognition and evaluation of an intraarticular knee effusion is important in differentiating the possible causes of knee pain. Important aspects of the history and physical are listed in Tables 1 and 2 respectively.

General treatment. The majority of knee pain responds to ice, analgesics, NSAIDs, leg flexibility and strengthening exercises (Tables 4 and 5). Many knee conditions will improve with conservative treatment consisting of low impact activities and exercises to improve muscular strength and flexibility (Table 4). In most cases a home treatment program should be explained in detail to the patient, including specific guidelines for activity modification and exercises. Initially, formal physical therapy is usually not required.

Failure to respond to a home program should prompt a re-evaluation of the initial diagnosis. Consultation with formal physical therapy is indicated if the clinician believes that lack of progress is due to an inability of the patient to correctly engage in the home program and would benefit from supervision.

Drug Treatment

Drug overview. Acetaminophen remains the first choice analgesic in patients with mild to moderate knee osteoarthritis. Patients who respond poorly to acetaminophen should be given a trial of traditional NSAIDs unless the patient has a documented intolerance to traditional NSAIDs, or has risk factors for GI bleeding, such as: (1) a history of upper GI bleeding, (2) receiving chronic, high dose systemic corticosteroids, or (3) presence of a bleeding disorder. In these cases a trial of a COX-2 inhibitor is indicated. Celecoxib is contraindicated in sulfa-allergic patients. COX-2 inhibitors should be used with

caution in patients at high risk for atherosclerotic disease until further studies clarify the potential risks.

Data on topical capsaicin and oral glucosamine and/or chondroitin are limited, but encouraging for the symptomatic treatment of mild to moderate knee osteoarthritis. Glucosamine and chondroitin have minimal side effects, and are therefore potentially appealing agents. Ongoing large trials will hopefully allow for definitive recommendations regarding these agents.

Acetaminophen & NSAIDs. The American College of Rheumatology recommends acetaminophen as the initial pharmacologic agent for the treatment of knee osteoarthritis. This recommendation is based on the similar efficacy of high dose acetaminophen (4000 mg/day) compared to traditional NSAIDs and the lower side effect profile. More recent studies indicate that traditional NSAIDs may be modestly more efficacious than acetaminophen in patients with severe knee osteoarthritis. Both acetaminophen and NSAIDs are analgesics with no disease modifying effect.

COX-2 Inhibitors. Traditional NSAIDs should be recommended over COX-2 inhibitors in most patients UNLESS: 1) the patient has a history of upper GI bleeding, 2) the patient is receiving chronic, high dose systemic corticosteroids, 3) the patient is receiving anticoagulants, 4) the patient has bleeding disorders, 5) the patient has a documented intolerance to traditional NSAIDs. COX-2 inhibitors are significantly more expensive than acetaminophen or ibuprofen (see Table 6).

Selective cyclooxygenase 2 (COX-2) inhibitors were developed to decrease the adverse effects on the GI-tract found in traditional NSAIDs that block both COX-1 and COX-2. Multiple studies have found that COX-2 inhibitors are superior to placebo in treating symptomatic knee osteoarthritis. No major studies demonstrate greater efficacy of COX-2 inhibitors over traditional NSAIDs. Longer duration studies are needed to judge the long term effectiveness of COX-2 inhibitors and determine the risk/benefit ratio for long term use.

When patients taking a COX-2 inhibitor were compared to patients taking traditional NSAIDs, short-term (6 months) gastrointestinal side effects were less, but were no different

at one year follow up. Differences in the rate of serious GI side effects are most pronounced in patients with a history of peptic ulcer and gastrointestinal bleeding.

Analyses of the major trials of COX-2 inhibitors demonstrate an increase in cardiovascular event rates for patients taking COX-2 inhibitors. Rofecoxib (Vioxx) was withdrawn from the market in 9/2004 and valdecoxib (Bextra) in 4/2005 by the manufacturers due to evidence that they increase risk of cardiovascular events. Traditional NSAIDs should be used in preference to COX-2 inhibitors unless conditions warranting the use of COX-2 inhibitors are present (see Table 7). COX-2 inhibitors should usually be avoided in patients with cardiac risk factors.

Glucosamine and chondroitin. Glucosamine and chondroitin extracts from animal tissue have been available in food supplements in Europe for 20 years and have recently become very popular in the United States. Formulations containing glucosamine and chondroitin are considered food supplements in the USA and are not regulated by the FDA. Therefore, the potency, purity, safety and efficacy of products containing glucosamine and chondroitin are not tested. Typical recommended doses are 500 mg of glucosamine sulfate three times a day and 400 mg of chondroitin sulfate three times a day.

Several clinical trials have reported that glucosamine decreased pain and improved function in patients with knee OA significantly greater than placebo, and probably comparable to non-steroidal anti-inflammatory drugs (NSAIDs). It is not clear if glucosamine therapy can help repair damaged articular cartilage. Chondroitin also appears to have a favorable effect on knee OA pain, but relatively few quality studies have been published. The National Institute of Health has recently funded a large double-blinded randomized placebo controlled trial evaluating glucosamine and chondroitin therapies for knee OA. The results of this trial will hopefully clarify the efficacy and role of these agents in the treatment of knee OA.

Both glucosamine and chondroitin appear to be quite safe with few side effects, particularly in comparison to NSAIDs. The chondroitin sulfate molecule is similar in structure to heparin, and may interact with anti-coagulation medications. Neither agent has been studied in rheumatoid arthritis, gout, or traumatic knee pain.

Hyaluronic acid (HA). Hyaluronic acid, glucosamine and chondroitin are components of normal articular cartilage that have been promoted as treatments for knee osteoarthritis (OA). HA has been approved for treatments of pain in knee OA by the Federal Drug Administration (FDA) and is available in 2 products: Hyaluronate sodium (**Hyalgan**) and Hylan GF-20 (**Synvisc**). Each are injected intra-articularly into the knee weekly for 3-5 weeks. The theory behind HA treatment is that synovial fluid viscosity is decreased in knee OA. “Viscosupplementation” with HA is purported to improve joint lubrication, restore synovial

fluid viscosity, retard cartilage deterioration, and reduce pain.

Clinical trials evaluating the efficacy of HA injections in reducing pain are difficult to interpret because of the large and prolonged placebo effect seen with intra-articular injections. None of the five published prospective trials to date have shown HA injections in osteoarthritis to be superior to placebo. There is no evidence currently that HA injections repair damaged articular cartilage or modify the progression of osteoarthritis in humans. HA injections may be offered for patients refractory to other therapies who cannot or do not wish to undergo arthroplasty [D].

Adverse effects with intra-articular HA injections occur in about 8% of patients and are limited usually to a mild, self-limiting local reaction. The average wholesale price (AWP) for a single-use syringe of **Hyalgan** is \$150 and for **Synvisc** is \$235, making these therapies quite expensive.

Knee Pain and/or Swelling without Constitutional Symptoms (Figure 1)

Knee pain as the presenting symptom of underlying hip pathology is particularly common in children. Hip problems such as fracture, infection, avascular necrosis of the femoral head, or slipped capital epiphysis in a skeletally immature patient can present as knee pain.

Vascular Occlusion and Acute Injury. It is important to rule out serious causes of knee pain such as vascular occlusion and acute injury during the initial evaluation. To assess for vascular occlusion check for arterial pulses (popliteal, dorsalis pedis, posterior tibialis), temperature and lower extremity swelling and pain. Patients with knee pain and signs or symptoms of acute venous or arterial occlusion require immediate evaluation with vascular studies (non-invasive arterial Doppler studies or venous Doppler / IPG / venogram). Immediate vascular surgery consultation may be necessary, especially for acute arterial occlusion. Of those patients who have acute onset of knee pain secondary to acute injury, the differential diagnosis focuses on internal derangements such as fracture, dislocation, meniscal, or ligamentous injury. Further evaluation of internal derangements is presented in Figure 3. After ruling out trauma and vascular occlusion, the differential diagnoses of knee pain in patients without constitutional symptoms includes patellofemoral syndrome, osteoarthritis, prepatellar bursitis, inflammatory arthritis, Baker’s cyst and deep venous thrombosis.

Patellofemoral syndrome. Patellofemoral syndrome is the most common cause of atraumatic knee pain in patients under the age of 40. It is the result of abnormal patellofemoral tracking. It can result in chondromalacia patella, patellar subluxation, and patellofemoral arthritis. Predisposing conditions include vastus medialis weakness, foot pronations, valgus knee alignment (“knock-kneed”), tight hamstring muscles and iliotibial band. Repetitive knee flexion and extension activities (e.g., up and down stairs,

frequent squatting) will often cause patellofemoral pain. The pain is localized to the patellar region as opposed to the medial, lateral or posterior aspect of the joint. The goals of treatment are to improve patellofemoral tracking, reduce pain and retard development of arthritis with knee strengthening exercises, lower leg muscle stretching, and medication.

Osteoarthritis. If pain is not localized to the patellar region, the differential diagnoses includes degenerative meniscus and osteoarthritis. Osteoarthritis of the knee is a form of degenerative arthritis. Predisposing conditions include obesity, family history, previous meniscectomy, and genu valgum and genu varum. Treatment goals include losing weight if overweight, low impact exercises (Table 4) and medication to control pain. Randomized controlled trials have shown that acetaminophen and topical capsaicin cream effectively reduce pain in patients with osteoarthritis. There is no evidence that NSAIDs are more efficacious than acetaminophen in decreasing osteoarthritis pain.

If the pain is disabling, patients should be referred to a musculoskeletal specialist for evaluation of a torn meniscus or severe arthritis. If the pain is not disabling, a trial of conservative management is appropriate (activity restriction, analgesics, low impact exercises and quadriceps strengthening, return appointment within 3-4 weeks if unimproved for possible reevaluation or consultation).

Prepatellar swelling. Patients with chronic repetitive trauma (e.g., kneeling), anterior knee pain and swelling may have prepatellar bursitis. Aspiration of a prepatellar bursal effusion may be necessary to exclude the possibility of septic bursitis. Aspiration is only indicated if there is a history of skin disruption (e.g., abrasion, puncture wound) or the patient is immunocompromised (e.g., diabetes, chronic prednisone therapy, chemotherapy). Immunocompromised patients may have septic prepatellar bursitis even in the absence of direct inoculation.

The following recommendations related to white blood cell count are based on expert opinion.

- Patients with prepatellar bursal swelling and a high aspirate white blood count (>10,000) should receive antibiotic treatment and close follow-up to ensure resolution, parenteral antibiotics may be indicated for some patients (e.g., if patient is febrile, diabetic, or exhibiting overlying cellulitis).
- If the aspirate white blood count is between 2,000 and 10,000, send for crystal exam. If infection is suspected, send for culture and treat empirically with antibiotics.
- If the aspirate white blood count is very low (<2,000), or there is no indication to aspirate, then the patient most likely has a traumatic bursitis which will respond to conservative management such as activity modification to avoid direct trauma, knee padding, extension splints, and NSAIDs.

Intraarticular swelling. Patients without constitutional symptoms who have intraarticular swelling should have the effusion aspirated to help establish diagnosis and guide therapy (see Figure 4). Aspiration may not be necessary in patients with chronic effusions with known cause (e.g., osteoarthritis).

Posterior knee swelling. The differential diagnosis of posterior knee swelling includes a “Baker’s” or popliteal cyst or deep vein thrombosis (DVT). The etiology of popliteal cysts depends upon the age of the patient. In children under age 12, the swelling usually represents distention of the normally present gastrocnemius-semimembranosus bursa due to acute or repetitive trauma. It is rarely associated with intraarticular pathology, and therefore can be treated conservatively with avoidance of trauma. In adults, however, the fluid usually comes from the knee joint due to joint pathology. The most frequently associated conditions are osteoarthritis and degenerative menisci. The diagnosis of popliteal cyst is usually made by ultrasound. Treatment should be directed at the underlying condition.

Juvenile rheumatoid arthritis (JRA) in the pediatric population. JRA occurs in up to 0.1% of the pediatric population. Most of these patients present with no constitutional symptoms, and over 80% of these patients will have knee involvement. Any child presenting with acute onset of knee pain and swelling needs an x-ray, followed by arthrocentesis to exclude infection. Most children with chronic arthritis (as evidenced by swelling and bony changes on exam) do not require a repeat arthrocentesis. Consider referring JRA patients to a pediatric rheumatologist for evaluation, initiation of therapy, assessment of school/social needs and physical therapy.

Knee Pain with Constitutional Symptoms (e.g., fever, night sweats, malaise) (Figure 2)

The chances of infection or neoplasm are increased for patients with knee pain and constitutional symptoms. It is important to perform an x-ray on all patients, particularly younger patients, when there are constitutional symptoms. Primary or metastatic bone tumors of the knee are more commonly seen in younger patients (age < 18). Tumors are rare causes of knee pain, but must be considered in order to avoid errors in treatment that could result in loss of limb or even life. It is the opinion of the guideline team that prior to aspiration of a knee effusion, it is important to perform an x-ray in younger patients and any patient when there are constitutional symptoms. If the x-ray suggests the presence of neoplasm, then aspiration is not undertaken because limb salvage surgery may be an option for these patients. If neoplasm is ruled out, then aspiration should be performed to avoid delays in diagnosis and treatment of joint infection or crystalline synovitis (Figure 4).

For patients with knee pain and constitutional symptoms, a CBC and sedimentation rate are recommended in the initial

evaluation. If CBC and sedimentation rates are normal, then the patient may need to be reassessed to determine if patient symptoms are due to hip injury or other cause. Diseases such as subacute bacterial endocarditis, systemic vasculitis, sarcoidosis, and inflammatory bowel disease can initially present with localized joint pain, but usually the ESR is elevated when these conditions are present. If any of these conditions are suspected, further evaluation is appropriate.

For children (<18 years), it is important to check a CBC with platelets and peripheral smear to look for evidence of hematologic malignancy, such as leukemia, or profound anemia or thrombocytopenia suspicious for other malignancy affecting the bone marrow, such as stage IV neuroblastoma or lymphoma. These and other malignancies of childhood can present with referred pain to the knee and legs.

Traumatic Knee Pain (Figure 3)

Patients with acute or chronic trauma to the knee may result in an internal derangement injury. These patients may or may not have a joint effusion. Examples of internal derangements include menisci, cruciates, and chondral cartilage tears.

With Effusion. The age of the patient may influence the overall approach. In each age group, aspiration of a joint effusion for pain relief and/or to rule out bloody effusion is indicated. In patients with a bloody knee aspirate, internal derangement is extremely likely, and consultation with orthopedic evaluation is suggested. In non-bloody aspirates, a synovial fluid cell count and culture may reveal an infectious cause. In patients with significant loss of motion (e.g., 30-40%), orthopedic consultation should be considered (Figure 4).

For patients with minimal loss of motion, non-impact exercises may be undertaken as patient comfort permits. Many patients will improve over the next several weeks. Consultation may be necessary for patients whose knee problems persist or become chronic.

Without Effusion. It is the opinion of the guideline team that in cases of internal derangement, if the patient is younger than 50 years of age and the range of motion is nearly normal, an x-ray may not be required and low impact exercises can be initiated as soon as possible to prevent muscular atrophy. For patients younger than 50 years of age who have range of motion less than 90 degrees or who cannot bear weight, x-rays are indicated. If the x-ray reveals a fracture or loose fragment, consult with orthopedics. If the x-ray is normal, non-impact exercises should be undertaken. In older patients (50 years or older), x-rays are indicated if there is any point tenderness or pain that is disabling. If x-rays are normal or only show mild joint space narrowing, a trial of conservative treatment with low impact activity and muscle strengthening and flexibility exercises is indicated. Consider consultation with a

musculoskeletal specialist if pain persists or the patient is unable to engage in an appropriate exercise program or other activities.

Knee Effusion Not Grossly Bloody (Figure 4)

Patients with knee pain and swelling who have non-bloody aspirates may have serious underlying knee pathology. Causes of such problems include infection, crystalline synovitis, inflammatory conditions, non-inflammatory conditions and miscellaneous connective tissue diseases. Synovial fluid should be sent for cell count (see below) and other tests as indicated.

Positive gram stain. If the aspirated synovial fluid reveals a positive gram stain, the patient will require immediate blood culture and parenteral antibiotics.

Synovial fluid crystals. If polarizing microscopy reveals crystals of gout or pseudogout, immediate treatment is highly effective. Most patients are adequately treated with indomethacin 25 to 50 mg po qid maximum, tapering over five days with follow-up by the primary care physician or rheumatologist. Patients unable to take indomethacin may be able to tolerate other NSAIDs. Patients with a history of intolerance to NSAIDs or recent upper gastrointestinal bleeding may be treated by colchicine. Colchicine dosing is complex and requires careful patient education and a review of colchicine contraindications. Intraarticular steroid administration is one of the better alternative treatment strategies for acute gouty arthritis. Because crystalline arthritis and septic arthritis can occur together, clinical judgment and/or synovial fluid cell count and culture should be used to assure the absence of infection. Prior to intraarticular steroid administration, it is important to determine there is no contraindication to intraarticular steroid administration and there is sufficient benefit to be gained. If the crystalline attack is already well established, intraarticular steroid administration may be of little benefit. The treatment of pseudogout crystalline synovitis is similar in that excellent responses are usually observed to NSAIDs or colchicine. Consider further evaluation by rheumatology for patients with contraindications to these treatments.

Synovial fluid WBC/mm³. The threshold ranges presented below are based on expert opinion and are provided for general guidance only. Any specific clinical procedure or treatment must be made by the physician in light of all of the circumstances presented by the patient.

- **Synovial fluid WBC/mm³ less than 2,000.** These are considered bland synovial effusions. Bland or noninflammatory synovial effusions are frequently observed in patients who have trauma, osteoarthritis, degenerative joint disease, erythema nodosum, and "synovitis", but also occasionally in systemic diseases such as lupus or sarcoidosis. These patients should be considered for a trial of low impact exercise therapy and leg strengthening as tolerated. If these patients are unimproved over a course of six to twelve weeks, the initial diagnosis should be reevaluated. Formal physical

therapy consultation may be helpful and consultation with a musculoskeletal specialist may also be warranted.

- **Synovial fluid WBC/mm³ between 2,000 and 30,000.** These patients generally have inflammation and may have connective tissue diseases such as rheumatoid arthritis, lupus, scleroderma, dermatomyositis, polymyositis, or mixed connective tissue disease. Other possibilities include seronegative spondyloarthropathies (e.g., ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome and enteropathic arthritis or the arthritis of inflammatory bowel disease). Some forms of septic arthritis can have synovial fluid white blood count less than 30,000 (e.g., gonococcus, fungal and mycoplasma infections). Also, synovial fluid and white blood count may be decreased in immunocompromised patients.

There are approximately two hundred different types of arthritis which can be difficult to diagnose with certainty. Consultation with a rheumatologist should be considered if there is difficulty in determining the diagnosis or managing the inflammatory arthritis. In the setting of an inflammatory arthritis, if the patient is not severely disabled conservative measures such as acetaminophen, NSAIDs and exercise therapies may be attempted by the primary care physician. If symptoms are refractory or persistent after two to six weeks, rheumatology evaluation should be considered.

- **Synovial Fluid WBC/mm³ greater than 30,000** are highly inflammatory. Such high white blood cell counts in synovial fluid may be seen in septic arthritis, osteomyelitis, fungal and tuberculous arthritis, crystalline synovitis and rheumatoid arthritis, psoriatic arthritis and Reiter's syndrome. The first priority is to determine whether septic arthritis or other infectious problems such as endocarditis exist. Parenteral antibiotics, pending the results of blood and joint cultures, is the recommended course of action if infection is suspected. If the clinician does not suspect septic arthritis, conservative therapy may be appropriate if immediate follow-up can be assured over the next twenty-four to seventy-two hours.

Strategy for Literature Search

The literature search was conducted prospectively using the major keywords of: knee injuries, knee, patellofemoral, patello, anterior cruciate ligament, meniscus, meniscal tear, osteoarthritis, brace(s), immobilizer, immobilization, rehabilitation, x-rays, computed tomography, radiography, magnetic resonance imaging, MRI, diagnosis, treatment, randomized controlled trial, clinical trials, controlled clinical trial(s), meta-analysis, multicenter studies, comparative study(ies). Articles between 1976 and December 1996 were examined. The search was supplemented with recent clinical trials known to expert members of the panel. Negative trials were specifically sought.

Literature searches on three new topics were used to update the guideline: COX-2 inhibitors (cyclooxygenase inhibitors), hyaluronic acid, and glucosamine/chondroitin sulfates. Publications from July 1996 through available in April 2000 were examined. The following main terms were included in each of the three searches: knee, knee joint, knee medical collateral ligament, knee injuries, patella-injuries, knee-injuries, knee osteoarthritis, osteoarthritis, pain. Searches also included the following terms to identify the type of information provided: guidelines, clinical trials, and costs. (Specific MeSH search terms are available upon request.)

The search was a single cycle. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

Related National Guidelines

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

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Annotated References

Brandt KD, Smith GN, Simon LS. Intraarticular injection of hyaluronan as treatment for osteoarthritis. What is the evidence? *Arthritis & Rheumatism* 43:1192-1203, 2000.

A literature review of the therapeutic and disease modifying effects of hyaluronic acid.

Puett DW, Griffin MR. Published trials of nonmedicinal and noninvasive therapies for hip and knee osteoarthritis

[see comments]. *Ann Intern Med* (1994 Jul 15) 121(2):133-40.

A review article (English-language literature from 1966 through 1993) of the efficacy of nonmedicinal, noninvasive therapies in hip and knee osteoarthritis. Studies report that exercise reduces pain and improves function in patients with osteoarthritis of the knee. No support exists in the literature for pre-exercise ultrasound treatment. Single, well-designed studies suggest that topically applied capsaicin and laser treatment reduce pain associated with knee osteoarthritis. Data on three other therapies were sparse (transcutaneous electrical nerve stimulation, pulsed electromagnetic fields) or inconsistent (acupuncture).

McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA* 2000;283:1469-1475.

A meta-analysis of randomized controlled trials showing moderate effects compared to placebo.

Fischer SP, Fox JM, Del Pizzo W, Friedman MJ, Snyder SJ, Ferkel RD. Accuracy of diagnoses from magnetic resonance imaging of the knee. A multi-center analysis of one thousand and fourteen patients. *J Bone Joint Surg* 1991;73(1):2-10.

Magnetic resonance images of the knee were made for 1014 patients, and the diagnosis was subsequently confirmed arthroscopically. The accuracy of the diagnoses from the imaging was 89 per cent for the medial meniscus, 88 per cent for the lateral meniscus, 93 per cent for the anterior cruciate ligament, and 99 per cent for the posterior cruciate ligament. The magnetic resonance examinations were done at several centers, and the results varied substantially among centers. The accuracy ranged from 64 to 95 per cent for the medial meniscus, from 83 to 94 per cent for the lateral meniscus, and from 78 to 97 per cent for the anterior cruciate ligament.

Stiell IG, Greenberg GH, et al., Prospective validation of a decision rule for the use of radiography in acute knee injuries. *JAMA* 1996;275(8):611-615.

A prospectively administered survey to validate a previously derived decision rule for the use of radiography in patients with acute knee injury. The decision rule was found to be 100% sensitive for identifying fractures of the knee, and to allow physicians to reduce the use of radiography in patients with acute knee injury.

Smith BW, Green GA. Acute knee injuries: part I - history and physical exam. *American Family Physician* 1995;51(3):615-806.

A thorough review of history, physical and differential diagnoses for examinations of acute knee injuries.

Silverstein FE, Faich G, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. [see comments]. *JAMA*. 284(10):1247-55, 2000 Sep 13.

Celecoxib, a COX-2-specific inhibitor, is associated with a lower incidence of significant upper GI toxic effects and other adverse effects compared with conventional NSAIDs (respective rates of 2.1% vs 3.5% for the combination of symptomatic ulcers and GI ulcer complications).

Bombardier C, Laine L, et al. VIGOR Study Group. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. *New England Journal of Medicine*. 343(21):1520-8, 2 p following 1528, 2000 Nov 23.

In patients with rheumatoid arthritis, treatment with rofecoxib, a selective inhibitor of cyclooxygenase-2, is associated with significantly fewer clinically important upper gastrointestinal events than treatment with naproxen, a nonselective inhibitor (2.1 events/100 patients and 4.5 events/100 patients, respectively).