Osteoarthritis

By

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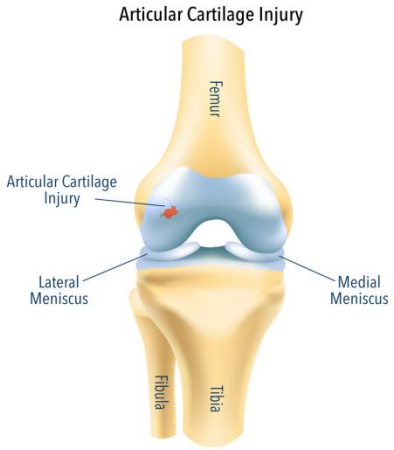
Osteoarthritis

- Osteoarthritis (OA) is a common, progressive **disorder affecting primarily weight-bearing joints**, characterized by progressive **destruction of articular cartilage**, osteophyte formation, pain, limitation of motion, deformity, and disability.

Pathophysiology

- **Primary (idiopathic) OA, the more common type, has no known cause**. **Secondary OA is associated with a known cause** such as inflammation, trauma, metabolic or endocrine disorders, and congenital factors.
- **OA usually begins with damage to articular cartilage** through injury, excessive joint loading from obesity or other reasons, or joint instability.

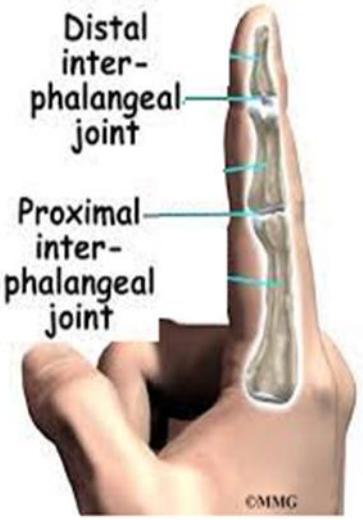


- Damage to cartilage **increases activity of chondrocytes** in attempt to repair damage, leading to increased synthesis of matrix constituents **with cartilage swelling**.

- Cartilage loss causes **joint space narrowing** and painful, deformed joints. **New bone formations (osteophytes**) at joint margins distant from cartilage destruction are thought to help stabilize affected joints.
- **Inflammatory changes can occur in the joint capsule and synovium**. Crystals or cartilage shards in synovial fluid may contribute to inflammation. Interleukin-1, prostaglandin E2, tumor necrosis factor-α, and nitric oxide in synovial fluid may also play a role. **Inflammatory changes result in synovial effusions and thickening**.
- Pain may result from distention of the synovial capsule by increased joint fluid; microfracture; or damage to ligaments, synovium, or the meniscus.

Clinical presentation

- **Risk factors include** increasing age, obesity, sex, certain occupations and sports activities, history of joint injury or surgery, and genetic predisposition.
- **The predominant symptom** is deep, aching pain in affected joints. Pain accompanies joint activity and decreases with rest.
- **Joints most commonly affected are** the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of the hand, first carpometacarpal joint, knees, hips, cervical and lumbar spine, and first metatarsophalangeal (MTP) joint of the toe.



- Limitation of motion, stiffness, **crepitus**, and deformities may occur. Patients with lower extremity involvement may report weakness or instability.
- Upon arising, **joint stiffness typically lasts less than 30 minutes** and resolves with motion. Presence of warm, red, and tender joints suggests inflammatory synovitis.
- Physical examination of affected joints reveals **tenderness**, **crepitus**, and possibly enlargement. bony enlargements (osteophytes) of the DIP and PIP joints, respectively.

Diagnosis

- Diagnosis is made through patient **history**, **physician examination**, **radiologic** findings, and **laboratory testing**.
- American College of Rheumatology criteria for classification of OA of the hips, knees, and hands include presence of **pain**, **bony changes on examination**, **normal erythrocyte sedimentation rate** (ESR), and **radiographs showing osteophytes** or joint **space narrowing**

Treatment

- **Goals of Treatment**:
- (**1**) Educate the patient, family members, and caregivers;
- (**2**) relieve pain and stiffness;
- (**3**) maintain or improve joint mobility;
- (**4**) limit functional impairment
- (**5**) maintain or improve quality of life.

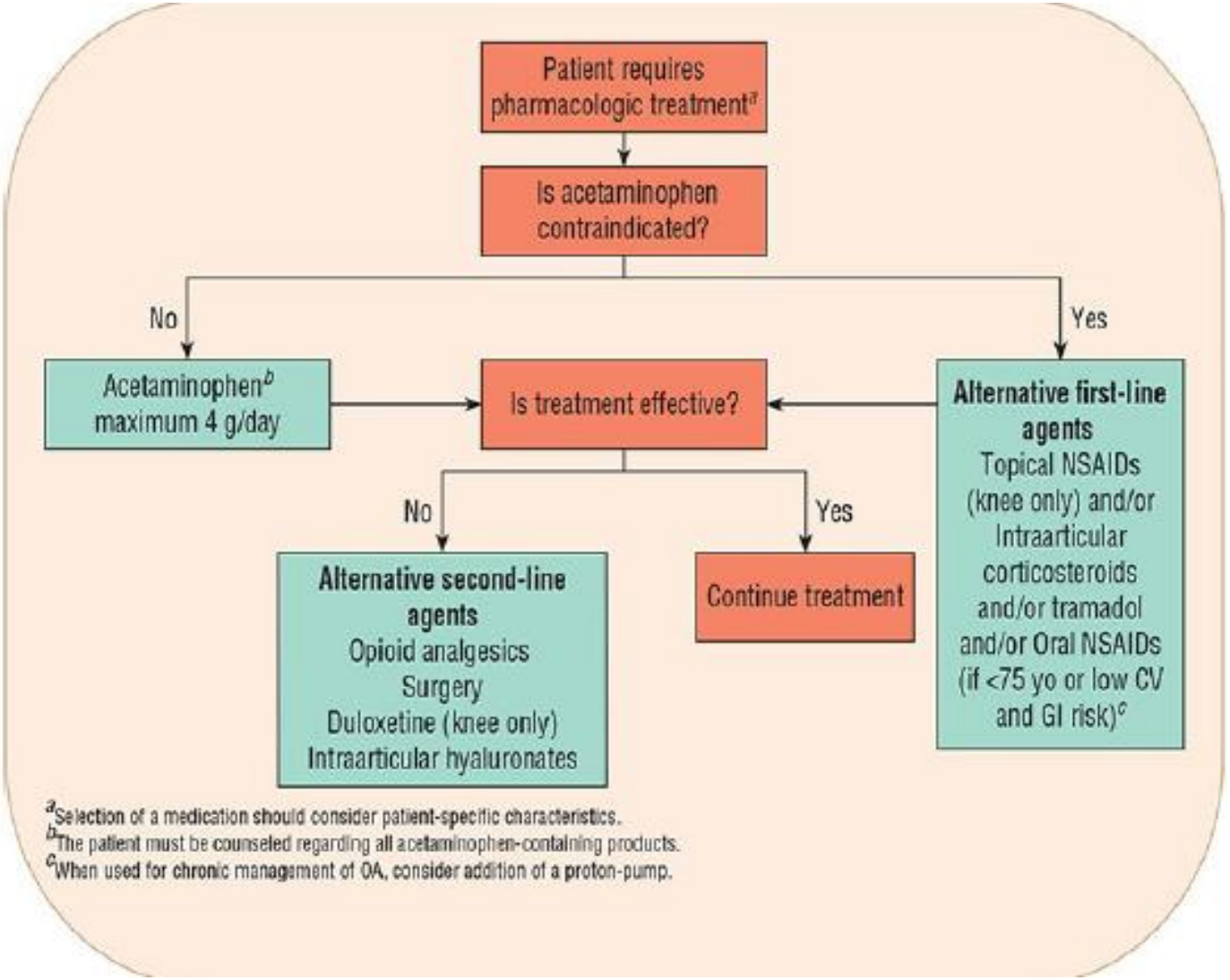
Nonpharmacologic Therapy

- **Educate** the patient about the disease process and extent, prognosis, and treatment options. Promote dietary counseling, exercise, and a weight loss program for overweight patients.
- **Physical therapy**—with heat or cold treatments and an exercise program—helps maintain range of motion and reduce pain and need for analgesics.
- **Assistive and orthotic devices** (canes, walkers, braces, heel cups, and insoles) can be used during exercise or daily activities.
- **Surgical procedures** (eg, osteotomy, arthroplasty, joint fusion) are indicated for functional disability and/or severe pain unresponsive to conservative therapy

Pharmacologic Therapy

- **General Approach**
- **Drug therapy is targeted at relief of pain**. Apply an individualized approach (Figs. 1 and 2). **Continue appropriate nondrug therapies when initiating drug therapy**.

Treatment recommendations for knee and hip osteoarthritis.



- **Knee and Hip OA**
- **Acetaminophen** is a **preferred first-line treatment**; it may be less effective than oral NSAIDs but has a lower risk of serious gastrointestinal (GI) and cardiovascular (CV) events.
- Acetaminophen is usually well tolerated, but potentially fatal **hepatotoxicity** with overdose is well documented. **It should be avoided in chronic alcohol users or patients with liver disease.**
- Nonselective NSAIDs or cyclooxygenase-2 (COX-2) selective inhibitors (eg, celecoxib) are recommended **if a patient fails acetaminophen**.

- Nonselective NSAIDs may cause minor GI complaints such as nausea, dyspepsia, anorexia, abdominal pain, and diarrhea. **They may cause gastric and duodenal ulcers** and bleeding through direct (topical) or indirect (systemic) mechanisms.
- **Risk factors for NSAID-associated ulcers and ulcer complications** (perforation, gastric outlet obstruction, and GI bleeding) **include** longer duration of NSAID use, higher dosage, age older than 60 years, past history of peptic ulcer disease of any cause, history of alcohol use, and concomitant use of glucocorticoids or anticoagulants.
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- Options for reducing the GI risk of nonselective NSAIDs include using (1) the **lowest dose** possible and only when needed, (2) **misoprostol** four times daily with the NSAID, and (3) a **PPI** or full-dose **H2-receptor antagonist** daily with the NSAID.
- **COX-2 inhibitors** pose **less risk for adverse GI events** than nonselective NSAIDs, but this advantage is substantially **reduced for patients taking aspirin**. **Both nonselective and selective NSAIDs are associated with an increased risk for CV events** (hypertension, stroke, myocardial infarction, and death).

- NSAIDs may also cause kidney diseases, hepatitis, hypersensitivity reactions, rash, and CNS complaints of drowsiness, dizziness, headaches, depression, confusion, and tinnitus. NSAIDs inhibit COX-1–dependent thromboxane production in platelets, thereby **increasing bleeding risk.**
- Unlike aspirin, **celecoxib and nonspecific NSAIDs inhibit thromboxane formation reversibly, with normalization of platelet function 1–3 days after drug discontinuation**. Avoid NSAIDs in late pregnancy because of risk of premature closure of the ductus arteriosus.

- The most potentially serious drug interactions include use of NSAIDs with lithium, warfarin, oral hypoglycemics, methotrexate, antihypertensives, angiotensin-converting enzyme inhibitors, β-blockers, and diuretics.
- **Topical NSAIDs are recommended for knee OA if acetaminophen fails**, and they are preferred over oral NSAIDs in patients older than 75 years.
- Topical NSAIDs provide **similar pain relief with fewer adverse GI events** than oral NSAIDs but may be associated with adverse events at the application site (eg, dry skin, pruritus, and rash).
- **Patients using topical products should avoid oral NSAIDs** to minimize the potential for additive side effects. Use of topical NSAIDs has not been linked with increased risk of CV events.

corticosteroid injections

- **Intra-articular (IA) corticosteroid injections** are recommended for both hip and knee OA **when analgesia with acetaminophen or NSAIDs is suboptimal**. They can provide excellent pain relief, particularly when joint effusion is present.

Local anesthetics

- **Local anesthetics** such as lidocaine or bupivacaine are commonly combined with corticosteroids to provide rapid pain relief. Injections may also be given with concomitant oral analgesics for additional pain control. **Local adverse effects** can include infection, osteonecrosis, tendon rupture, and skin atrophy at the injection site.
- Do not administer injections more frequently than **once every 3 months** to minimize systemic adverse effects. **Systemic corticosteroid therapy is not recommended in OA**, given lack of proven benefit and well-known adverse effects with long-term use

Opioid therapy

- **Tramadol** is recommended for hip and knee OA in patients who have failed scheduled full-dose acetaminophen and topical NSAIDs, who are not appropriate candidates for oral NSAIDs, and who are not able to receive IA corticosteroids

- **Tramadol can be added to partially effective** acetaminophen or oral NSAID therapy. Tramadol is associated with opioid-like adverse effects such as nausea, vomiting, dizziness, constipation, headache, and somnolence.
- However, tramadol is not associated with life-threatening GI bleeding, CV events, or renal failure. **The most serious adverse event is seizures**. Tramadol is classified as a Schedule IV controlled substance due to its potential for dependence, addiction, and diversion.
- There is increased risk of **serotonin syndrome** when tramadol is used with other serotonergic medications, including duloxetine.

- Opioids should be considered in patients **not responding adequately** to nonpharmacologic and first-line pharmacologic therapies. Patients who are at high surgical risk and cannot undergo joint arthroplasty are also candidates for opioid therapy.
- Use opioid analgesics in the lowest effective dose and the smallest quantity needed. **Avoid combinations of opioids and sedating medications whenever possible**. Inform patients on how to use, store, and dispose of opioid medications.
- **Assess opioid use at least every 3 months**, evaluating patient progression toward functional treatment goals, risks of harm, and adverse effects.

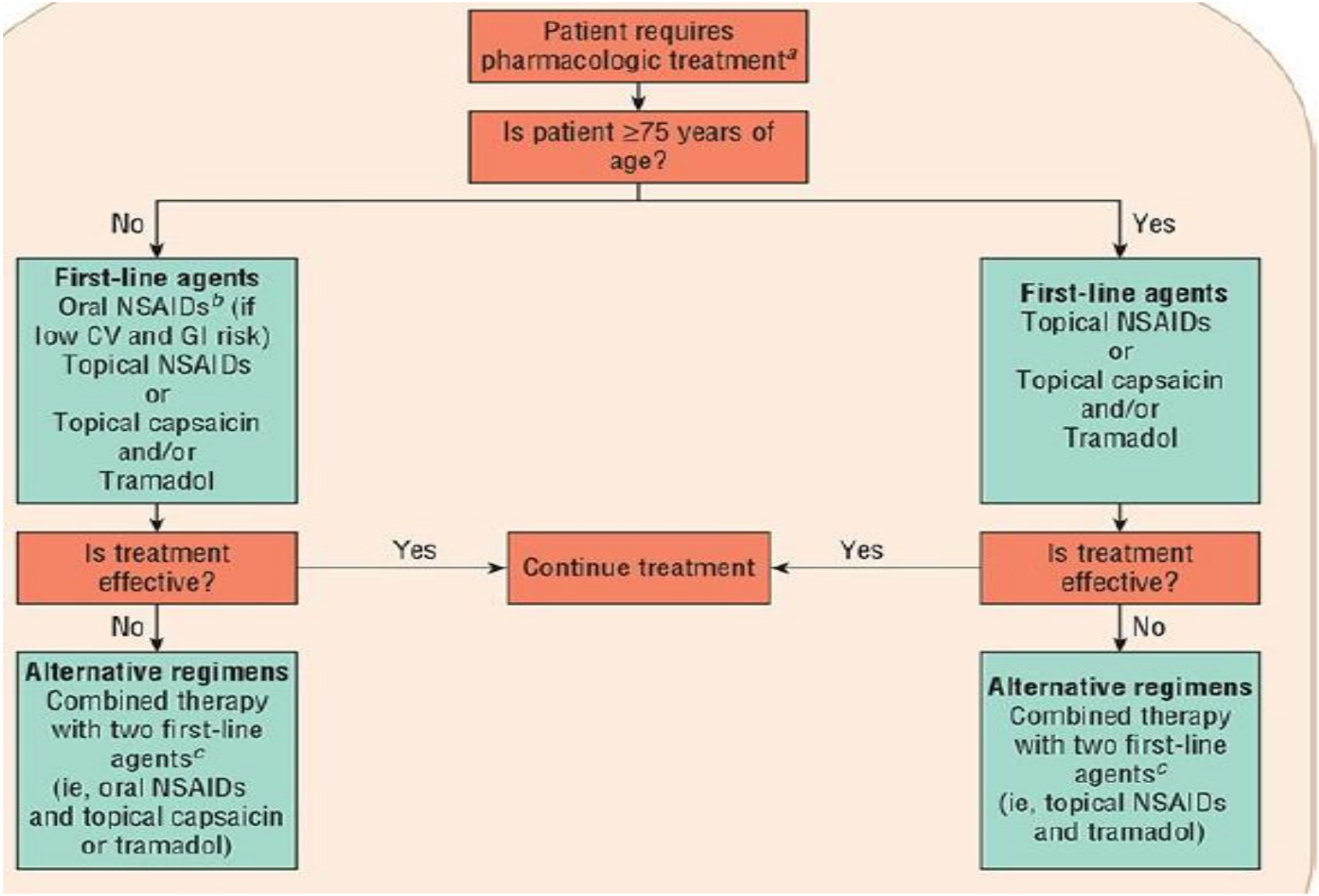
SSRI

- **Duloxetine** can be used as adjunctive **treatment of knee** (not hip) OA in patients with partial response to first-line analgesics (acetaminophen, oral NSAIDs).
- **It may be a preferred second-line medication in patients with both neuropathic and musculoskeletal OA pain**. Pain reduction occurs after about 4 weeks of therapy. Duloxetine may cause nausea, dry mouth, constipation, anorexia, fatigue, somnolence, and dizziness.
- Serious rare events include **Stevens-Johnson syndrome and liver failure**. Concomitant use with other medications that increase serotonin concentration (including tramadol) increases risk of serotonin syndrome.

hyaluronic acid

- **IA hyaluronic acid (sodium hyaluronate)** is not routinely recommended because injections have **shown limited benefit for knee OA and have not been shown to benefit hip OA.**
- Injections are usually well tolerated, but acute joint swelling, effusion, stiffness, and local skin reactions (eg, rash, ecchymoses, or pruritus) have been reported.
- **Glucosamine and/or chondroitin** and topical **rubefacients** (e.g, methyl salicylate, trolamine salicylate) lack uniform improvement in pain control or functional status for hip and knee pain and are not preferred treatment options.
- **Glucosamine** adverse effects are mild and include flatulence, bloating, and abdominal cramps. The most common adverse effect of chondroitin is nausea.

Hand OA


Patient requires pharmacologic treatment[a]
Is patient ≥75 years of age?
No
Yes
First-line agents
Oral NSAIDs[b] (if low CV and GI risk)
Topical NSAIDs
or
Topical capsaicin
and/or
Tramadol
First-line agents
Topical NSAIDs
or
Topical capsaicin
and/or
Tramadol
Is treatment effective?
Yes
Continue treatment
Yes
Is treatment effective?
No
No
Alternative regimens
Combined therapy with two first-line agents[c]
(ie, oral NSAIDs and topical capsaicin or tramadol)
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Combined therapy with two first-line agents[c]
(ie, topical NSAIDs and tramadol)

- **Topical NSAIDs are a first-line option for hand OA**. **Topical diclofenac** has efficacy similar to oral NSAIDs with fewer adverse GI events, albeit with some local application site events. Efficacy with topical NSAIDs typically occurs with 1–2 weeks.
- **Oral NSAIDs** are **an alternative first-line treatment** for patients who cannot tolerate the local skin reactions or who received inadequate relief from topical NSAIDs.
- **Capsaicin cream** is **an alternative first-line treatment**. It is a reasonable option for patients unable to take oral NSAIDs. Capsaicin must be used regularly to be effective, and it **may require up to 2 weeks to take effect**. Adverse effects are primarily local and include burning, stinging, and/or erythema that usually subsides with repeated application. Warn patients not to get cream in their eyes or mouth and to wash hands after application. Application of the cream, gel, solution, or lotion is recommended four times daily.

- Tramadol is **an alternative first-line treatment** and is a reasonable option for patients who do not respond to topical therapy and are not candidates for oral NSAIDs because of **high GI, CV, or renal risks**.
- Tramadol may also be used **in combination with partially effective** acetaminophen, topical therapy, or oral NSAIDs.

Evaluation of therapeutic outcomes

- Obtain baseline **serum creatinine**, **hematology profile**, and **serum transaminases** with repeat levels at **6- to 12-month intervals** to identify specific toxicities to the kidney, liver, GI tract, or bone marrow.
- **Ask patients about adverse effects from medications**