

OSTEOARTHRITIS

Introduction

When the student has completed this module, he/she will be able to:

1. Identify possible causes of osteoarthritis.
2. Identify the basic pathological process of osteoarthritis.
3. Identify two common sites of osteoarthritis.
4. Identify self-help measures that can help people with osteoarthritis.
5. Identify signs and symptoms of osteoarthritis.
6. Identify at least three drugs that are used to treat osteoarthritis.
7. Identify a side effect (respectively) of the non-steroidal anti-inflammatory drugs and the COX-2 inhibitor drugs.
8. Identify the two basic methods used to diagnose osteoarthritis.
9. Identify two surgical techniques that can be used to treat osteoarthritis.
10. Identify an indication for total joint replacement.

Epidemiology

Osteoarthritis (OA) is a very common disorder, the most common disorder of the joints in the United States.¹ Osteoarthritis of the knee and the hip occurs in approximately 6% and 3% of the population 30 years of age and older, and the incidence of the disease increases with advancing age: some studies have noted an incidence of OA of the knee as high as 37% in the population 60 years of age and older, and studies on cadavers have shown that structural OA changes are almost universal in the elderly.

From 1995 to 2005, the number of people afflicted with OA has grown from 21 million to 27 million, and as the population of the United States gets older and the percent of the population that is obese increases, this number is expected to grow: one source estimates that the prevalence of osteoarthritis will increase 66% to 100% by the year 2020.²

Etiology/Risk Factors

There is no single etiological cause responsible for OA. Rather, OA develops through an incompletely understood, complex interaction between individual and environmental factors that, along with normal (and often times, abnormal) joint loading, causes a gradual diminishing of the protective mechanisms that keep the joints healthy and increases the vulnerability of the joints to the disease.

Learning Break: A more basic explanation for OA is that it is often simply a part of aging that happens to older adults with bad genetics who, usually, are overweight.

Age/Gender

There is no doubt that, as mentioned previously, age is an important risk factor for the development of OA: why this is so is not exactly clear. However, it is known that weight bearing stimulates the growth and strength of the cartilage in younger people, but this response decreases as we age and our cartilage gets thinner as we get older. Also, the muscles, tendons, and ligaments that surround, support, and protect the integrity of the joints weaken and stretch with advancing years, putting more stress on the joints.³

OA is much more common among middle-aged and elderly women; it is not known why this is so.

Genetics

Familial aggregation studies (studies that examine the incidence of a disease in families) and twin studies (studies that examine the incidence of a disease in monozygotic and dizygotic twins) have shown that there is strong evidence for a genetic contribution to the development, progression, and severity of OA.⁴ Twin studies have shown a heritability for OA of the hand, hip, and knee in women ranging from 39% to 65%, and other studies have shown a heritability for disease progression.⁵ Genes may be involved in OA by influencing the biomechanics of the joints, by causing joint deformity and/or muscle weakness, by influencing bone density, vascularity of the joint, or the inflammatory response to stress and injury, or by obesity.⁶

Obesity

Obesity is clearly an important risk factor for OA of the knees, and there is also evidence – not conclusive – that it is a risk factor for OA of the hip. A body mass index (BMI) over 30 can increase the risk of developing OA of the knee by more than four to seven-fold. As well, obesity is strongly associated with a faster progression of the disease.

Learning Break: It is not completely clear why obesity helps cause OA, but obese people often have gait abnormalities that add stress to the joints and the extra weight, over time, may damage cartilage. Obese people also have high levels of inflammatory cytokines, and there is evidence that OA is, in part, an inflammatory process.

Pathophysiology of OA

The pathologic changes of OA in affected joints are complex. Initially, the cartilage that lines the joints and provides cushioning between bony surfaces begins to erode in a patchwork fashion and eventually the cartilage wears away and bone meets bone. As this process continues, degenerative changes in the adjacent bone and damage to the joint capsule and surrounding structures, e.g., muscles occur, and the patient with OA is left with a joint that is stiff, weak, and painful.

Signs and Symptoms of OA

OA can be a very serious condition and can severely affect activities of daily living (ADL). It affects many joints, although not all. The most common sites for OA are the hip, knee, hands, cervical and lumbar vertebrae, and the first metatarsal phalangeal joint. The wrist, elbow, and ankle are usually not affected. Pain that is exacerbated by activity and relieved by rest is the hallmark of OA, but at times, the pain can occur at rest.⁷ The typical signs and symptoms of OA include:⁸

- Tenderness of the joint
- Crepitus with movement of the joint
- Reduced range of motion
- Joint deformity
- Joint instability
- Reduced function
- Stiffness of the joint
- Altered gait

For the sufferer of OA, pain is the most important and debilitating aspect of the disease, but it is not completely clear what causes the pain of OA. The muscles, ligaments, tendons, synovium, subchondral bone, and articular capsule all have a large nerve supply, but the joint cartilage is aneural.

Learning Break: OA pain is probably caused by inflammation of the synovium, bone marrow edema, and effusions into the joint.

OA is usually diagnosed through clinical examination and the history of the patient's complaints. X-rays will confirm the diagnosis; laboratory tests are not used except to differentiate OA from rheumatoid arthritis.

TREATMENT

Unfortunately, there is no cure for OA and the therapeutic options available do not change the progression of the disease. The goal for treatment then is to try and help the patient manage the pain and to perform his/her activities of daily living without significant interruption.

Exercise and Weight Loss

The patient with OA can definitely make lifestyle changes that will be helpful. He/she will need to be aware of the activities that cause pain and avoid or change these. Exercise that strengthens the muscles around the joint can be useful. When these muscles are strong, joint stability will be improved and there will be less stress placed on the joint. Studies have shown that for patient with OA of the knee, exercise decreases pain and improves function. Certainly, succumbing to the pain of OA by becoming more sedentary will not be helpful; muscle strength is very important for joint protection and the weaker the muscles surrounding a joint, the more susceptible that joint will be to injury.

Losing weight is very important. As mentioned previously, obesity is a strong risk factor for OA.

Learning Break: An increase of one pound of bodyweight increases the load on the knees by three to six-fold.⁹

Drug Therapy

Drug therapy is probably the most commonly used approach for the treatment of OA. Of course, all drugs have side effects and not all drugs are for all patients.

- **Acetaminophen** is a commonly used and effective over-the counter analgesic for relieving mild to moderate OA pain, and it compares favorably in this respect to the nonsteroidal anti-inflammatory drugs (NSAIDs).^{10,11} It is the first-line drug recommended by the American College of Rheumatology.¹² The exact mechanism by which acetaminophen works is not known. The drug is usually well tolerated and the side effects are minimal: gastrointestinal upsets can be seen but other side effects are rare or not definitively associated with acetaminophen. The drug has a rapid onset of effect – one hour – and the duration of pain relief is usually 4-6 hours. Although there have been many studies that have shown that acetaminophen is very effective for treating mild to moderate OA pain, some researchers feel that because there is an anti-inflammatory component to OA, acetaminophen –which does *not* have anti-inflammatory properties –can be less effective than the NSAIDs.¹³
- **Tramadol** is a non-narcotic analgesic that binds to opioid receptors and interferes with the reuptake of norepinephrine and serotonin. It appears to be a stronger drug than acetaminophen and can be used to treat moderate to severe OA pain,^{14,15} but there is evidence that its effectiveness is not great and its use should be restricted to people who cannot tolerate NSAIDs or for whom their use is contraindicated.¹⁶ Tolerance and central nervous system depression are common side effects.
- **Nonsteroidal anti-inflammatory drugs** work by inhibiting the synthesis of prostaglandins, lipid compounds that have many functions, including mediating – and in the case of OA, decreasing - inflammation. They have anti-inflammatory and analgesic effects and are commonly prescribed for the relief of pain from OA. There are six major classes of the NSAID drugs, they differ in their properties, and it may take some trial and error to find the one best suited for any particular individual. Unfortunately, the side effects make the NSAIDs difficult to tolerate and in some cases, medically risky. Gastrointestinal pain is relatively common and the risk of serious gastrointestinal effects (e.g., peptic ulcer, bleeding, and perforation) has been estimated to be 3.5% to 4.7%. Some of the gastrointestinal upsets can be prevented by misoprostol and proton-pump inhibitors, but the H2 blockers have not been shown to have a prophylactic effect.¹⁷ Nephrotoxicity is also possible with NSAIDs: according to one author, approximately 1% to 5% of patients taking an NSAID develop a clinically significant renal abnormality and

people with liver disease, congestive heart failure, diabetes, hypertension, and several other medical disorders are at especially at risk.¹⁸

Learning Break: The risk of gastrointestinal bleeding from the NSAID drugs is worse in patients over the age of 60, patients with a history of gastrointestinal bleeding, and for patients who are taking high doses.

Learning Break: Although OA is not considered to be *primarily* an inflammatory condition, there is some evidence that inflammation in the bone and synovial structure may be a cause of the pain of OA.

- **Selective cyclooxygenase inhibitors** (aka COX-2 inhibitors) are a class of NSAIDS that were developed in an attempt to provide pain relief for patients with OA while decreasing the gastrointestinal complications of the other NSAIDS: celecoxib/Celebrex™ is one of the commonly prescribed drugs of this class. They work by selectively inhibiting COX-2, an enzyme that is needed for the production of a specific prostaglandin that mediates inflammation and pain. They differ from the traditional NSAIDS in that they selectively inhibit the COX-2 enzyme, whereas the other NSAIDS inhibit (to a degree that differs with each drug) both COX-2 and COX-1. As COX-1 is an enzyme used to produce a prostaglandin that protects the integrity of the gastrointestinal tract, its inhibition by the traditional NSAIDS can cause the gastrointestinal side effects. The COX-2 inhibitors can be an effective treatment for OA pain,¹⁹ but renal problems are still possible and the American College of Cardiology has stated that the COX-2 inhibitors should be prescribed very cautiously in patients who have, or who are at risk for, cardiovascular disease, as the use of these drugs has been associated with serious cardiac events, e.g., myocardial infarction.²⁰
- **Topical agents** have been used to relieve the pain of OA and some of these have been successful. Topical diclofenac (an NSAID) has been shown in several studies to relieve OA pain of the hands and knees,^{21,22} and topical ibuprofen (an NSADI) can be effective, as well.²³ There are many over-the-counter salicylate-containing topical solutions available. They supposedly reduce OA pain by increasing local blood flow, but these products have not been specifically studied in patients with OA and where they have been noted to work, the effect has been short-lived and rated moderate to poor.²⁴ Capsaicin-containing creams have an oil that is extracted from pepper plants and they are commonly used for musculoskeletal pain. Capsaicin works by causing local skin irritation, which in turn causes a neurologic stimulation that decreases substance P in the nerve fibers. Substance P is a neurotransmitter that mediates pain, so if there is less substance P, pain will be decreased. Several studies have shown that these creams are effective if they are used 3 to 4 times a day for 3 to 4 weeks.^{25,26} Capsaicin can cause skin irritation, especially if it is applied to mucous membranes. Topical lidocaine has been successfully used for treating OA of the spine.²⁷

- **Glucosamine** is an endogenous compound that is involved in the synthesis of proteoglycans, polysaccharide-protein conjugates that are essential building blocks of articular cartilage. **Chondroitin** is also a normal component of animal cartilage. Glucosamine has been used (often along with chondroitin) since the '80s for treating OA pain – it is thought that it can prevent cartilage loss and possibly even enhance cartilage synthesis - and it is a very popular drug, generating millions of dollars in sales each year. However, there is a *lot* of conflicting information on the efficacy of this drug for treating OA (this appears to be due to methodological problems with the studies) and some professional organizations recommend its use – or at least suggest trying it - and some don't. (e.g., American College of Rheumatology). The side effects of glucosamine are usually minimal (gastric distress), but it is possible that for certain patients with diabetes, insulin resistance may be increased.^{28,29}

Learning Break: One of the largest and most well known studies of glucosamine/chondroitin was the Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT). GAIT concluded that glucosamine/chondroitin was no more effective than a placebo, but it was also noted that GAIT and most of the research that examined the effectiveness of glucosamine/chondroitin has methodological problems that limit the conclusions that can be drawn.

- Intra-articular injections of corticosteroids have been used for many years for the symptoms of OA.^{30,31} OA is not primarily an inflammatory process, but there is some evidence that inflammation contributes to the pain and triamcinolone and methylprednisolone can be effective pain relievers.³²

Learning Break: Although intra-articular injections of corticosteroids have been shown to be effective in the short-term (one week) relief of OA pain, but there is no evidence supporting long-term benefits,³³ and the injections may be damaging to cartilage.³⁴

- **Hyaluronic acid** is a naturally occurring substance that acts as a “cementing agent” that gives skin and other body tissues tone and volume. Hyaluronic acid injections can relieve the pain of OA, possibly by inhibiting the activity of catabolic enzymes that damage matrix substances in cartilage.³⁵ However, although some patients find the injections helpful there is not enough evidence at this time to definitively state that hyaluronic acid is a useful treatment for OA; in several large studies, a placebo was just as effective as hyaluronic acid and there may be a greater risk of adverse effects when compared to other treatments.^{36,37}

Acupuncture

Some authors have reported success using acupuncture for the treatment of OA pain³⁸ while others have reported conflicting evidence for efficacy.³⁹ Regardless, acupuncture is essentially safe, relatively inexpensive, and widely available.

Nutritional Supplements

There has been much interest in the role of nutrition in both the pathogenesis of OA and in treating the disease. Selenium, vitamin D, and vitamin K deficiencies have all been identified as possible risk factors for developing OA, but there is no definitive evidence that a lack of these nutrients can cause OA. Beta carotene, vitamin E, and vitamin C may possibly slow the progression and relieve the symptoms of OA, but they don't seem to prevent its occurrence.^{40,41}

Learning Break: There is some intriguing evidence that suggests that diet may play a role in the development and progression of OA and that nutritional supplements – especially antioxidants - could be useful, but at this point, there is no proof that dietary deficiencies are major risk factors or that supplementation is a viable treatment option.

Braces and Supportive Devices

Canes and walkers can be very helpful for patients with OA and canes have been shown to reduce the load on the hip by 50%.⁴² Realignment unloader braces, patellar bracing and taping, and insoles can also be used and these have been successful, although not all patients will get pain relief.⁴³

Surgery

Surgery is an option for patients with OA, and the treatments range from minimally invasive, e.g., arthroscopy, to total joint replacement.

- Arthroscopy for OA of the knee that included debridement and lavage was the standard of care for many years, but in 2002, it was shown that this procedure was no better than placebo.⁴⁴ Currently, arthroscopy is used for patients with mild to moderate osteoarthritis who have a large tear in the meniscus or a loose body; the procedure corrects mechanical derangements, it is not a cure for the OA. Hip arthroscopy is not often performed for patients with OA.
- Osteotomy (the removal of bone) can help correct misalignment and adjust joint loading. Most of the time, this procedure is performed on younger patients who are active and athletic instead of a total joint replacement because strenuous sports activities can cause premature failure of the replacement.⁴⁵
- Joint replacement (arthroplasty) is a very commonly performed procedure. Total hip replacement is performed for patients with pain that significantly interferes with ADL. OA destruction of the knee is the commonest reason for total knee replacement.

SUMMARY

OA is very common and as the population continues to get older, it will be an even bigger public health care problem. Many patients can manage the disease with lifestyle alterations, e.g., weight loss, exercise, and avoiding painful activities. Some patients will need to add a medication to this treatment regimen and for others, the painful and disruption of the disease is so intense that surgery is needed. There is ongoing research to find drugs that will actually alter the course of the disease and possibly prevent it, but at this time, there are no commercially available products.⁴⁶

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