Continuing pharmaceutical education (CPE) program

Alexandria Syndicate of pharmacists

Musculoskeletal injuries

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Musculoskeletal injuries & disorders (MSDs)

Other synonyms for MSDs are cumulative trauma disorders (CTDs), repetitive strain injuries (RSIs) and overuse injuries.

Function of the human musculoskeletal system:
The musculoskeletal system's primary functions include supporting the body, allowing motion, and protecting vital organs. The skeletal portion of the system (bones) serves as the main storage for calcium and phosphorus and contains critical components of the hematopoietic system (bone marrow).

Components of human musculoskeletal system:
The musculoskeletal system includes the muscles, bones, tendons, ligaments, joints, cartilages, and other connective tissue. Muscles are attached to bones by tendons, and ligaments connect bone to bone. Tendons and ligaments rarely rupture unless subjected to intense forces due to their tensile force, but can be damaged when subjected to overuse. Cartilage functions as protective pads between bones in joints and vertebral column. Skeletal or striated muscle (voluntary) is composed of myocytes in which 2 constituents (actin & myosin) are primarily responsible for contraction. Muscle contraction also involves several electrolytes within the muscle tissue such as Ca\(^{+2}\) and K\(^+\).

Pain receptors are located in skeletal muscles & fascia and can be stimulated by overuse or injury to the muscle or surrounding tissue.

Musculoskeletal disorders (MSDs):
MSDs are one of the most common human complaints in pharmacy. They affect all age groups (especially geriatrics) and frequently cause disability, impairments, and handicaps. They consist of a variety of different diseases that cause pain (called musculoskeletal pain) or discomfort in the bones, joints, muscles, nerve or surrounding structures, and they can be acute or chronic, local, or diffuse.

MSDs maybe idiopathic, iatrogenic or related to injury. The development of MSDs can be acute such as acute soft-tissue injuries “STIs” (sprains & strains) or chronic such as pain from osteoarthritis (OA) and rheumatoid arthritis (RA).
Signs & symptoms of MSDs:
Pain is the most common symptom among all MSDs. There are other symptoms according to each case such as numbness, loss range of motion, stiffness......etc.

Pain scale
Patient self-rating of pain on a scale of zero (no pain) to 10 (worst possible pain). Used to assess pain both at rest and with movement. Determined at baseline and to assess response to therapy.

Referred pain
Musculoskeletal pain maybe felt in the affected tissue itself or referred from another part of musculoskeletal system such as hip pain is referred from its primary source of in the low back. Sometimes, pain that seems to be musculoskeletal is actually caused by a disorder in another organ system. For example, shoulder pain may be caused by a disorder affecting the spleen or gallbladder. Arm pain may be caused by a heart attack (myocardial infarction “MI”).

Erythema, edema and tenderness at the affected site characterize the inflammatory response. The initial injury exposes membrane phospholipids to phospholipase A₂, leading to the formation of arachidonic acid which is transformed by cyclooxygenase (COX) to thromboxanes and prostaglandins (PGs), including PGE₂. PGE₂ is the most potent inflammatory mediator; it increases vascular permeability, leading to redness, warmth, and swelling of the affected area.

Sprains:
A sprain is a stretched or torn ligament. Falling, twisting or getting hit can cause a sprain. Ankle and wrist sprains are the most common types. There are 3 grades of sprains:
Grade I results from excessive stretching
Grade II results from partial tear
Grade III involves complete tear of the tissue

Strains:
A strain is a stretched or torn muscle or tendon. Tendons are tissues that connect muscle to bone. Twisting or pulling these tissues can cause a strain.
Non-pharmacological therapy consist of RICE:
Rest
Ice
Compression
Elevation
Guidelines for RICE therapy

- Rest the injured area and continue until pain is reduced (generally 1-2 days). Slings, splints or crutches can be used if necessary
- Apply ice as soon as possible to the injured area in 10-15 minutes increments, 3-4 times daily. Continue the ice-pack therapy for 1-3 days, depending on the severity of the injury.
- Apply compression to the injured area with an elastic support or an elasticized bandage
- Elevate the injured area at or above the level of the heart 2-3 hours a day to decrease swelling and to relieve pain

Low back pain (LBP) or lumbago:
This is the most common type of MSDs. It is important to understand that LBP is not a distinct medical condition but a symptom caused by numerous medical illnesses and conditions. Low back pain may be classified by the duration of symptoms as acute (less than a month) and chronic (more than 3 months).

Causes of lower back pain are varied. Most cases are believed to be due to a sprain or strain in the muscles and soft tissues of the back. Overactivity of the muscles of the back can lead to an injured or torn ligament in the back which causes the pain. An injury can also occur to one of the intervertebral discs. Due to aging, discs begin to diminish and shrink in size, resulting in vertebrae and facet joints rubbing against one another.

Main risk factors for developing LBP includes:
- Sedentary lifestyle
- Poor posture
- Improper shoes
- Excessive body weight
- Sleeping posture
- Lifting heavy objects improperly

There are other causes of LBP includes congenital anomalies, OA, vertebral fractures, spinal tuberculosis and referred pain from diseased kidney, pancreas, liver or prostate.

Sciatica:
Refers to pain, weakness, numbness, or tingling in the leg. It is caused by injury to or pressure on the sciatic nerve. Sciatica is a symptom of another medical problem, not a medical condition on its own. Sciatica occurs when there is pressure or damage to the sciatic nerve. This nerve starts in the lower spine and runs down the back of each leg. This nerve controls the muscles of
the back of the knee and lower leg and provides sensation to the back of the thigh, part of the lower leg, and the sole of the foot.

**Neck pain:**

- Neck pain usually results from strains and sprains.
- It may shoot down an arm or cause a headache.
- Diagnosis based on symptoms, results of a physical examination, and sometimes x-rays or other imaging tests.
- Treatment includes taking pain relievers, applying ice or heat, wearing a **neck collar** (soft and hard), and learning how to stand, sit, and sleep to avoid straining the neck.

**Bursitis:**

It is an **inflammation** of the **bursa** (pleural: **bursae**), small fluid-filled sacs that can lie under a tendon, cushioning the tendon and protecting it from injury. The bursa assists with movement by reducing friction between joints to avoid wear and tear. Bursitis is a common cause of localized pain, tenderness and swelling which is worsened by any movement of the structure adjacent to the bursa, it generally results from either an acute injury to the joint or over-repetitive joint action.

**Tendonitis or tendinitis:**

It is the inflammation of a tendon, which results from acute injury or from chronic overuse of body part. Repetitive use of the tendon can cause cellular changes in the tissue leading to losing elasticity and its ability to handle stress or weight. This makes the tendon vulnerable to rupture or inflammation. Lastly **fluoroquinolone antimicrobial** agents have been suspected in the development of tendonitis and tendon rupture, and these medication carry a boxed warning. Patients older than 60 years who are taking steroids, or have had heart, lung, or kidney transplantation at high great risk.

**Carpal tunnel syndrome:**

Is a condition characterized by tingling or numbness of the first digits of the hand due to repetitive use of the hands and wrists. Other symptoms are sense of heat or cold, a sense that their hands are swollen when they are not, weakness and tendency to drop things. It is caused by the compression of the median nerve in the wrist.

Carpal tunnel syndrome is becoming more frequently recognized and may be occurring more often. It may result from repetitive motion or the use of devices like computer keyboards. It affects the median nerve, the nerve that supplies feeling and movement to the thumb and "thumb-side" of the hand. This tunnel is normally **narrow**, so any swelling can pinch the nerve and cause pain, numbness, tingling or weakness.
Carpal tunnel syndrome is common in people who perform repetitive motions of the hand and wrist. Typing on a computer keyboard is probably the most common cause of carpal tunnel. Other causes include:

- Sewing
- Driving
- Painting
- Writing
- Use of tools (especially hand tools or tools that vibrate)
- Sports such as racquetball or handball
- Playing some musical instruments

Patients with carpal tunnel syndrome often experience a sense of heat or cold, a sense that their hands are swollen when they aren’t. Symptoms persist during sleep and even when the hand is not being used. Treatment includes anti-inflammatory drugs, shots of corticosteroid into the carpal tunnel and finally carpal tunnel release (surgical procedure).

**Muscle cramp or spasm:**
A muscle cramp is a sudden, brief, usually painful contraction of a muscle or group of muscles. It can occur in healthy people (usually middle-aged and older people), sometimes during rest but especially during or after vigorous exercise. Some people have leg cramps during sleep. These painful cramps usually affect the calf and foot muscles, causing the foot and toes to curl downward.

Skeletal muscle relaxants such as baclofen (Mylobac®, Baclofen®), Chloroxazone (Flexofan®, Myolgin®, Myofen®), Tizanidine (sirdalud®, Rekan®) and methocarbamol. These agents should be used with caution because they all may cause sedation.

**Fibromyalgia:**
Fibromyalgia is a common syndrome in which a person has long-term, body-wide pain and tenderness in the joints, muscles, tendons, and other soft tissues. It has also been linked to fatigue, sleep problems, headaches, depression, and anxiety.

**Causes:**
The cause is unknown. Possible causes or triggers of fibromyalgia include:

- Physical or emotional trauma
- Sleep disturbances
- Infection, such as a virus.

**Symptoms:**
Pain is the main symptom of fibromyalgia. It may be mild to severe. Painful areas are called
tender points. Tender points are found in the soft tissue on the back of the neck, shoulders, chest, lower back, hips, shins, elbows, and knees. The pain may feel like a deep ache, or a shooting, burning pain. The joints are not affected, although the pain may feel like it is coming from the joints. To be diagnosed with fibromyalgia, you must have had at least 3 months of widespread pain, and pain and tenderness in at least 11 of 18 areas, including:

1. Arms (elbows)
2. Buttocks
3. Chest
4. Knees
5. Lower back
6. Neck
7. Rib cage
8. Shoulders
9. Thighs

Treatment

- Physical therapy
- Exercise and fitness program
- Stress-relief methods, including light massage and relaxation techniques

If these treatments do not work, there is pharmacological treatment such as an antidepressant or muscle relaxant. The goal of medication is to improve sleep and pain tolerance. Duloxetine belongs to a class of medications called selective serotonin and norepinephrine reuptake inhibitors (SNRIs) (Cymbalta®), pregabalin (Lyrica®), are medications that are approved specifically for treating fibromyalgia. However, many other drugs are also used to treat the condition, including:

- Anti-seizure drugs
- Other antidepressants
- Muscle relaxants
- Pain relievers
- Sleeping aids

General treatment approaches:

Non-pharmacological therapy:
Injury from playing sports or exercising is preventable by warming up and stretching muscle before physical activity, ensuring proper hydration, and not exercising to the point of exhaustion. For muscle cramps, stretching and massaging the affected area immediately followed by rest will loosen the muscle. For electrolyte depletion, appropriate oral
supplementation of wasted electrolytes can be used, with the selection of fluids containing Na\(^{+1}\), K\(^{+1}\) and Mg\(^{+2}\)

**Pharmacological therapy**

- **Systemic analgesics**
- **Topical products**

Localized pain maybe treated effectively with local topical therapy, whereas generalized pain is best treated with systemic agents.

**Systemic analgesics**

NSAIDs and acetaminphen (paracetamol) are commonly used nonprescription analgesics, and are often used in the initial treatment of MSDs. Acetaminphen is drug of choice for mild to moderate musculoskeletal pain without inflammation. It should be used with caution in patients with liver disease or consume alcohol due to risk of hepatotoxicity. Scheduled doses of nonprescription strengths are instituted early in the course of the injury. Followed by quick tapering of dose and interval as the injury improves. Analgesic therapy should be limited to 7 days of self care use, and patient should seek appropriate medical care if the condition continue beyond this period or worsen during the course of treatment.

Chronic use of nonselective NSAIDs leads to more severe and prevalent side effects such as **nephropathy**, **gastrointestinal ulceration** and **bleeding**.

![Diagram of COX-1 and COX-2 inhibition](Image)
Musculoskeletal injuries & disorders

Doses of NSAIDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial daily dose</th>
<th>Maximum Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>650mg every 4 hr</td>
<td>6000 mg</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>75mg twice a day</td>
<td>200 mg</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>400mg three times a day</td>
<td>3200 mg</td>
</tr>
<tr>
<td>Naproxen</td>
<td>1000mg twice a day</td>
<td>2000 mg</td>
</tr>
<tr>
<td>Celocoxib</td>
<td>100mg twice a day</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

Side effects of NSAIDs

- GIT effects: such as irritation, erosion of gastric mucosa, nausea, vomiting, and dyspepsia
- CNS effects: such as depression, drowsiness, headache, dizziness, visual disturbance, ototoxicity, and confusion
- Hematologic effects: such as thrombocytopenia, altered platelet function, and prolonged bleeding time
- Skin rash
- Nephrotoxicity

COX₂ inhibitors are approved for use in both RA and OA.

Cox 2 inhibitors appear to cause very little incidence of GIT ulceration or antiplatelet effects as nonselective NSAIDs

But many patients experienced gastrointestinal bleeding with this drugs soon after their release and this is thought to be due to overdosing of the drug

Nephrotoxicity exist for these drugs and the patients should be monitored for the change in renal function.

More recent adverse drug reactions associated with these drugs include an increased risk of thrombotic events, leading to myocardial infarction and stroke, which could be potentially fatal. This is likely the result of an inhibition of cardiovascular COX₂ and subsequent clot
formation. This has lead to the voluntary removal of some of these drugs (Rofecoxib and valdacoixib) from the market and cautious, closely supervised use of the others.

Other anti-inflammatory & anti-edematous agents

Alphintern®, Newbezime®, Flamogen®, Ambezime® have a synergistic, anti-inflammatory and anti-edematous action of two potent proteolytic enzymes “trypsin & chemotrypsin” affecting the exudative phase of inflammation and ensuring the destruction of peptidic chains in inflammatory processes regardless of the origin.

They are gastro-resistant and enteric-coated Tablets to ensure the best tolerance, as well as, the best efficiency due to its absorption in the intestine only.

There are also other dosage forms such as Maxilase® syrup and alpha chemotrypsin® ampoules

NO-NSAIDs:

Recently, a new class of nitric-oxide-releasing non-steroidal anti-inflammatory drugs (NO-NSAIDs) is being studied as safe NSAIDs because of their gastric-sparing properties. They have been designed, synthesized as prodrugs such as naproxcinod (nitronaproxen) is a NSAID developed by the French pharmaceutical company NicOx. It is a derivative of naproxen with a nitroxybutyl ester to allow it to also act as a nitric oxide (NO) donor. It undergoes phase III of clinical trials.

Topical products

Maybe analgesic, anesthetic or counterirritant. Some patient may prefer external analgesic to systemic analgesic because the rubbing during application can be comforting.

Counterirritants: are agents used to achieve pain relieving by producing a less severe pain to counter a more intense one. Counterirritants are classified into 4 classes according to their topical effects:

Group A: Rubefacients (produce redness): such as methyl salicylate and turpentine oil

Group B: produces cooling effect: such as menthol and camphor

Group C: produces vasodilation: methyl nicotinate

Group D: produces irritation only (no redness): capsicum, capsicum oleoresin ,capsaicin.
Methyl salicylate:
It occurs naturally as wintergreen oil. It is usually combined with antipruritic or analgesic properties such as camphor or menthol. It causes vasodilation of cutaneous vasculature producing reactive hyperemia. Because of this rubefacient action, it is responsible for the hot action in many topical counterirritant products.

studies on the rate and extent of percutaneous absorption various preparation containing methyl salicylate show direct tissue penetration, rather than redistribution by the systemic blood supply, indicating a localized effect of the topical product.

Capsaicin:
It relieves pain by stimulating the release of substance P from sensory nerve fibers, which ultimately depletes stores of substance P. The depletion occurs both peripherally and centrally. When substance P is released, burning pain occurs but disappears with repeated application. The initial burning sensation can lead to poor adherence, and health care providers should inform their patient’s about these effects and the importance of continuing therapy. Pain relieve is usually noted within 14 days after therapy has begun.

Once capsaicin has begun to relieve pain, its use must continue regularly 3 or 4 times a day to keep the pain from returning. Shouldn’t be applied to mucus membrane or any wound or damaged skin.

Myasthenia Gravis:
It is an autoimmune neuromuscular disease leading to fluctuating muscle weakness and fatiguability. It is caused by circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors throughout neuromuscular junctions. It is treated medically with acetylcholinesterase inhibitors or immunosuppressants.

The hallmark of myasthenia gravis is fatigability. Muscles that control eye and eyelid movement, facial expressions, chewing, talking, and swallowing are especially susceptible.

Effects of aging on musculoskeletal system:
Loss of muscle (sarcopenia) is a process that starts around age 30 and progresses throughout life. In this process, the amount of muscle tissue and the number and size of muscle fibers gradually decrease. The result of sarcopenia is a gradual loss of muscle mass and muscle strength. This mild loss of muscle strength places increased stress on certain joints (such as the knees) and may predispose a person to arthritis.

From about age 30, the density of bones begins to diminish in men and women. This loss of bone density accelerates in women after menopause. As a result, bones become more fragile and are more likely to break, especially in old age.
Osteoporosis:

Osteoporosis (means porous bones that is compressible like a sponge) is a disease of bones that leads to an increased risk of fracture. In osteoporosis the bone mineral density (BMD) is reduced, bone microarchitecture deteriorates, and the amount and variety of proteins in bone is altered.

Bones contain minerals, including Ca$^{+2}$ and PO$_4$, which make them hard and dense. To maintain bone density, the body requires an adequate supply of calcium and must produce the proper amounts of several hormones, such as parathyroid hormone (PTH), growth hormone (GH), calcitonin, estrogen, and testosterone. An adequate supply of vitamin D is also needed to absorb calcium from food and incorporate it into bones. Vitamin D is absorbed from the diet and also manufactured in the skin by sunlight.

There are 2 main types of osteoporosis: primary osteoporosis, which occurs spontaneously, and secondary osteoporosis, which is caused by another disorder or drug.

Primary Osteoporosis: More than 95% of osteoporosis in women and probably more than 80% in men is primary. Most cases occur in postmenopausal women and in older men. The terms postmenopausal, senile, and age-related osteoporosis have been used to describe this type of primary osteoporosis. A major cause of osteoporosis is a lack of estrogen, particularly the rapid decrease that occurs at menopause.

Secondary Osteoporosis: Examples of disorders that may cause secondary osteoporosis are chronic kidney failure and hormonal disorders (especially Cushing's disease, hyperparathyroidism, hyperthyroidism, hypogonadism, and diabetes mellitus). Examples of drugs that may cause secondary osteoporosis are corticosteroids (called glucocorticoid-induced osteoporosis “GIOP”), barbiturates, and anticonvulsants.

Osteoporosis itself has no specific symptoms; its main consequence is the increased risk of bone fractures. Osteoporotic fractures are those that occur in situations where healthy people would not normally break a bone (during normal activities); they are therefore regarded as fragility fractures. Typical fragility fractures occur in the vertebral column, rib, hip and wrist.

Diagnosis is done by DXA or DEXA (Dual-Energy “emission” X-ray Absorptiometry). It is a means of measuring bone mineral density (BMD). Two X-ray beams with differing energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone.

Treatment of osteoporosis:
Medications can be classified acc. to mechanism of action as:
Antiresorptive agents

I. Bisphosphonates (main pharmacological treatment)

They are the first-line therapy for postmenopausal osteoporosis due to established efficacy in preventing hip and vertebral fractures. They are called bisphosphonates because they have two phosphonate (PO$_3$) groups and are similar in structure to pyrophosphate. They decrease bone resorption by binding to bone matrix and inhibiting osteoclast activity

- Sodium alendronate (Fosamax®, Osteomepha®, Bonapex®)
  - 10 mg/day or 70 mg once a week
- Risedronate (Actonel®) 5 mg/day or 35 mg once a week
- Ibandronate (Bonviva®) once/month.
- Etidronate (Etidron®)
- Zoledronic acid (Zometa®) 5 mg infusion once/year for treatment of osteoporosis in men and post-menopausal women at increased risk of fracture.

○ Oral bisphosphonates are poorly absorbed, & must therefore be taken on an empty stomach, with no food or drink to follow for the next 30 min. They are associated with esophagitis and are therefore sometimes poorly tolerated; weekly or monthly administration decreases occurrence of esophagitis.

○ Parenteral bisphosphonate (zolendronate) avoids oral tolerance but they cause a rare but severe bone disease called osteonecrosis of the jaw.

II. Estrogen analogs

Estrogen replacement therapy “ERT” remains a good treatment for prevention of osteoporosis but is not recommended unless there are other indications for its use as well. There is a risk to develop breast and uterine cancer.

III. SERMs (Selective Estrogen Receptor Modulators)

Raloxifene (Evista®) is a partial agonist which act as antagonist on breast & uterine tissue and agonist on bones

IV. Calcitonine

It works by directly inhibiting osteoclast activity via the calcitonin receptor that present on the osteoclasts. It is produced from the parafollicular C- cells of the thyroid gland.
Bone anabolic agents

I. Teriparatide (Forteo®)

- It is a recombinant PTH has been shown to be effective in osteoporosis. It acts like PTH and stimulates osteoblasts. It is used mostly for patients with established osteoporosis, has very low BMD or can’t tolerate the oral bisphosphonates. It is given as a daily injection with the use of a pen-type injection device.

II. Calcium salts & vitamin D

Strontium ranelate (Protelos® sacchet)
It is an alternative oral treatment, belonging to a class of drugs called "dual action bone agents" (DABAs). It is taken as a 2 g oral suspension daily, and is used for the treatment of osteoporosis to prevent vertebral & hip fracture.

Osteoarthritis (OA):
OA is the most common form of arthritis. It is characterized by a gradual softening and destruction of the cartilage between bones. Cartilage and bone are destroyed in the joint spaces and regenerated, causing a rearrangement of the synovial architecture.

It is also called degenerative arthritis, degenerative joint disease, osteoarthrosis, or hypertrophic osteoarthritis. It is a chronic disorder associated with damage to the cartilage and surrounding tissues and characterized by pain, stiffness, and loss of function.

It is often begins in the 40s and 50s and affects almost all people to some degree by age 80. Before the age of 40, men develop osteoarthritis more often than do women, often because of injury. From age 40 to 70, women develop the disorder more often than do men. After age 70, the disorder develops in both sexes equally.

Osteoarthritis is classified as primary (or idiopathic) when the cause is not known (as in the large majority of cases). It is classified as secondary when the cause is another disease or condition, such as an infection, deformity, injury, abnormal use of a joint. The major risk factor for osteoarthritis of the knee comes from having an occupation that involves bending of the joint. Curiously, long-distance running does not increase the risk of developing the disorder. However, once osteoarthritis develops, this type of exercise often makes the disorder worse. Obesity may be a major factor in the development of osteoarthritis, particularly of the knee and especially in women.

Usually, symptoms develop gradually and affect only one or a few joints at first. Joints of the fingers, base of the thumbs, neck, lower back, big toes, hips, and knees are commonly affected.
Pain, often described as a deep ache, is the first symptom and, when in the weight-bearing joints, is usually made worse by activities that involve weight bearing (such as standing). In some people, the joint may be stiff after sleep (morning stiffness), but the stiffness usually subsides within 30 minutes, particularly if the joint is moved.

As the condition causes more symptoms, the joint may become less movable and eventually may not be able to fully straighten or bend. New growth of cartilage, bone, and other tissue can enlarge the joints. The irregular cartilage surfaces cause joints to crackle (crepitus sounds) when they are moved. Osteoarthritis often affects the spine. Back pain is the most common symptom. Usually, damaged disks or joints in the spine cause only mild pain and stiffness. However, osteoarthritis in the neck or lower back can cause numbness, pain, and weakness in an arm or leg if the overgrowth of bone presses on nerves.

Treatment of osteoarthritis

**Acetaminophen or paracetamol** (Panadol®, Abimol®) can relieve pain, but doesn’t reduce inflammation. It has been shown to be effective for people with osteoarthritis who have mild to moderate pain. Taking more than the recommended dosage of acetaminophen which is 4gm per day can cause hepatotoxicity.

**Nonsteroidal anti-inflammatory drugs (NSAIDs):** NSAIDs reduce inflammation and relieve pain. Over-the-counter NSAIDs include ibuprofen (Brufen®, Marcofen®, Profinal®) and naproxen (Naprofen®, Maxipan®). Stronger NSAIDs are available by prescription only.

**Narcotics:** only prescribed to provide relief from very severe osteoarthritis pain. These stronger medications carry a risk of dependence, though that risk is thought to be small in people who have severe pain. Side effects may include nausea, constipation and sleepiness.

**Physical therapy:** Referral to a physical therapist is very important if case needs it. The physical therapist can work with patient to create an individualized exercise regimen that will strengthen the muscles around the joint, increase the range of motion in the joint and reducing pain.

**Cortisone shots:** Injections of corticosteroid medications may relieve pain in joint. During this procedure doctor numbs the area around joint, and then inserts a needle into the space within joint and injects medication. The number of cortisone shots can receive each year is limited, because the medication can cause joint damage.

**Lubrication injections:** Injections of hyaluronic acid derivatives (Hyalgan, Synvisc) may offer pain relief in knee. These treatments are made of rooster combs and are similar to a
component normally found in your joint fluid. A series of 3 to 5 weekly injections of into the joint may provide significant pain relief in some people for prolonged periods of time (up to a year).

**Joint replacement:** In joint replacement surgery (arthroplasty), surgeon removes damaged joint surfaces and replaces them with plastic and metal devices called prostheses. The hip and knee joints are the most commonly replaced joints. Surgical risks include infections and blood clots. Artificial joints can wear out or come loose and may need to eventually be replaced.

**Nutritional supplements** (such as glucosamine sulfate and chondroitin sulfate) are being tested for potential benefit in treating osteoarthritis. So far, results are contradictory, and the potential benefit of glucosamine sulfate and chondroitin sulfate is unclear.

**Rheumatoid arthritis (RA):**
RA is a complex chronic systemic autoimmune disease that involves inflammation in the membrane lining of the joint (inflamed synovium) and often affects internal organs. The exact cause of rheumatoid arthritis is not known. Components of the immune system attack the soft tissue that lines the joints and can also attack connective tissue in many other parts of the body, such as the blood vessels and lungs. Eventually, the cartilage, bone, and ligaments of the joint erode, causing deformity, instability, and scarring within the joint. The joints deteriorate at a variable rate. Many factors, including genetic predisposition, may influence the pattern of the disease. Unknown environmental factors (such as viral infections) are thought to play a role.

Diagnosis and clinical evaluation: the American college of rheumatology “ACR” classifies RA by having at least 4 of the following 7 criteria, and the first 4 criteria must have been present for at least 6 weeks:

1. Morning stiffness for 1 hour
2. Arthritis of 3 or more joint areas of the hand, wrist, elbow and knee
3. Arthritis of hand joints with swelling
4. Symmetrical arthritis
5. Rheumatoid nodules
6. Serum rheumatoid factor is high
7. Radiological changes

**Treatment of rheumatoid arthritis:**
There is no cure for RA. Medications can reduce inflammation in order to relieve pain and prevent or slow joint damage. Occupational and physical therapy can teach the patient how to protect his/her joints. If the joints are severely damaged by rheumatoid arthritis, surgery may be necessary.

**NSAIDs:** mentioned before
Steroids such as prednisone (Hostacortin®) and prednisolone (Hostacortin® H), reduce inflammation and pain and slow joint damage. Side effects may include thinning of bones, cataracts, weight gain and diabetes. Doctors often prescribe a corticosteroid to relieve acute symptoms, with the goal of gradually tapering off the dose.

Non-biological disease-modifying antirheumatic drugs (DMARDs): These drugs can slow the progression of RA and save the joints and other tissues from permanent damage. Common DMARDs include methotrexate (Methotrexate®), leflunomide (Arthfree®), hydroxychloroquine (Plaquesnil®), sulfasalazine (Pentasa®, Salofalk®) and minocycline (Dynacin, Minocin, others). Side effects vary but may include liver damage, bone marrow suppression and severe lung infections.

The newest class of agents used as RA disease modifiers are biological DMARDs. These agents should be used only after failure of non-biological DMARDs. They can also reduce or prevent joint damage and preserve joint function.

TNF-alpha inhibitors: Tumor necrosis factor-alpha (TNF-alpha) is an inflammatory substance produced by body. TNF-alpha inhibitors can help reduce pain, morning stiffness, and tender or swollen joints. Examples are etanercept (Enbrel®), infliximab (Remicade®)

- **Abatacept** (Orenica®) is the first modulator of a co-stimulatory signal required for full T cell activation. It is used as monotherapy or concomitantly with non-biological DMARDs
- **Rituximab** is anti-CD20 monoclonal antibody. Depletion of CD20+B cells improve synovitis associated with RA. Severe, even fatal, infusion reactions have been reported.
- **Anakinra** is an IL-1 receptor antagonist. It is used as monotherapy or in conjunction with any DMARDs except a TNF blocker

Immunosuppressants: These medications act to tame immune system, which is out of control in rheumatoid arthritis. Examples include azathioprine (Imuran®, Azathioprine®), cyclosporine (Neoral®, Sandimmune®). These medications can increase susceptibility to infection.

Gout:
It is a disorder that results from deposits of urate crystals, which accumulate in the joints because of high blood levels of uric acid (hyperuricemia), leading to attacks of painful joint inflammation. Its is more common among men than women. Usually, gout develops during middle age in men and after menopause in women. Normally, uric acid, a by-product of cell nucleic acid breakdown, is present in small amounts in the blood because the body continually breaks down cells and forms new cells. Also, the body readily transforms substances in foods called purines into uric acid.
Foods high in purines include anchovies, asparagus, consommé, herring, meat gravies and broths, mushrooms, mussels, all organ meats, sardines, and sweetbreads.

Gout most often affects the joints in the feet, particularly at the base of the big toe (podagra). However, it also commonly affects other areas: the ankle, instep, knee, wrist, and elbow. Gout tends to affect these cooler areas because uric acid crystals form more readily in cool than in warm areas. Rarely, gout affects the joints of the warmer, central part of the body, such as the spine, hips, or shoulders.

**Symptoms**
Attacks of gout (acute gouty arthritis) can occur without warning. They may be triggered by an injury, surgery, consumption of large quantities of purine-rich food. Typically, severe pain occurs suddenly in one or more joints, often at night. The pain becomes progressively worse and is often excruciating, particularly when the joint is moved or touched. The joint becomes inflamed—it swells and feels warm, and the skin over the joint may appear red or purplish, tight, and shiny.

The first few attacks usually affect only one joint and last for a few days. The symptoms gradually disappear, joint function returns, and no symptoms appear until the next attack. However, if the disorder progresses, untreated attacks last longer, occur more frequently, and affect several joints. After repeated attacks, gout can become severe and chronic and may lead to joint deformity.

Hard lumps of uric acid crystals (tophi) are first deposited in the joint (synovial) lining or cartilage or in bone near the joints and then under the skin around joints.

**Treatment has 3 goals:**

- Relieve the acute attack of inflammation
- Prevent further attacks
- Prevent further deposition of uric acid in the tissues by lowering blood levels of uric acid

Relieving the Acute Attack: NSAIDs are often effective in relieving pain and swelling in the joint.

Colchicine is the traditional, but no longer the most common, first-step treatment. Usually, joint pain begins to subside after 12 hours of treatment with colchicine and is gone within 36 to 48 hours. Colchicine is usually taken in tablet form each hour until symptoms are relieved. Colchicine can cause abdominal pain and diarrhea. It can occasionally cause more serious side effects, including damage to the bone marrow.

Corticosteroids, such as prednisone, are sometimes useful to reduce joint inflammation in people who cannot tolerate the other drugs.
Diagnosis of musculoskeletal disorders:

- **Physical examination** done by a physician
- **Laboratory testing:**
  They are often helpful in making the diagnosis of MSDs. For example, the *erythrocyte sedimentation rate* (ESR) and *C-reactive proteins* are increased when inflammation is present. However, because inflammation occurs in so many conditions, the ESR alone does not establish a diagnosis. The level of *creatinine kinase* (a normal muscle enzyme that leaks out and is released into the bloodstream when muscle is damaged) may also be tested. Levels of creatine kinase are increased when there is widespread ongoing destruction of muscle.
  In rheumatoid arthritis, a blood test to identify rheumatoid factor or *anti-cyclic citrullinated peptide* (anti-CCP) antibody is helpful in making the diagnosis. *X-rays* are most valuable for detecting abnormalities in bone and are taken to evaluate painful, deformed, or suspected abnormal areas of bone. Often, x-rays can help to diagnose fractures, tumors, injuries, infections, and deformities. X-rays do not show soft tissues such as muscles, bursae, ligaments, tendons, or nerves.
- **Arthrography** is an x-ray procedure in which a radiopaque dye is injected into a joint space to outline the structures, such as ligaments inside the joint. Arthrography can be used to view torn ligaments and fragmented cartilage in the joint. However, MRI is now generally used in preference to arthrography.

**Drug induced musculoskeletal disorders**

Drug-induced MSDs can vary greatly from those that are asymptomatic biological abnormalities to severe and even life-threatening conditions.

Since a wide range of medicines can cause musculoskeletal symptoms, they should be always considered in the differential diagnosis of patients presenting with such symptoms. It can present as cramps, aches and pains in the limbs; this can be disabling, and can also be an early indication of potentially serious disorders.

The most common classes of drugs cause musculoskeletal symptoms are:

- **Statins** or **HMG-CoA reductase inhibitors** (lipid lowering agents) causes myopathy
- **Corticosteroids**
- **Retinoids**
- **Fluoroquinolones**
- **Biphosphonates**

**Medical terminology**
Myofascia pain originates from the fascia
Musculoskeletal pain originate from the muscle
Fibromyalgia: chronic pain syndrome characterized by diffuse muscle and joint pain, joint stiffness, fatigue, and sleep disturbances
Strain is injury to a muscle or tendon caused by overextension
Sprain is injury to the ligament caused by joint overextension
Muscle spasm is involuntary contraction of the muscle
Muscle cramp is prolonged muscle spasm that produce painful sensation
### Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>MSDs</td>
<td>Musculoskeletal disorders</td>
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<tr>
<td>CTDs</td>
<td>Cumulative trauma disorders</td>
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<td>RSIs</td>
<td>Repetitive strain injuries</td>
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<td>OA</td>
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<td>RA</td>
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<td>COX</td>
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<td>PGs</td>
<td>Prostaglandins</td>
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<td>NSAIDs</td>
<td>Nonsteroidal anti-inflammatory drugs</td>
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<td>DMARDs</td>
<td>Disease modifying antirheumatic agents</td>
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<tr>
<td>RICE</td>
<td>Rest, Ice, Compression, Elevation</td>
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<tr>
<td>HMG-CoA</td>
<td>Hydroxymethyl glutaryl CoA</td>
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<td>anti-CCP</td>
<td>anti-cyclic citrullinated peptide</td>
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<td>ESR</td>
<td>Erythrocyte sedimentation rate</td>
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<td>TNF alpha</td>
<td>Tissue necrosis factor alpha</td>
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<td>GIT</td>
<td>Gastrointestinal tract</td>
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<td>PTH</td>
<td>Parathyroid hormone</td>
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<td>GH</td>
<td>Growth hormone</td>
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- Webmed ([www.webmed.com](http://www.webmed.com))