

In the name of God

Musculoskeletal disorders and Management of pain

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- Osteoarthritis
- Myalgia
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- Carpal Tunnel Syndrome
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- Pain management



Overview Musculoskeletal disorders

Musculoskeletal disorders comprise diverse conditions affecting bones, joints, muscles, and connective tissues. These disorders may result in pain and loss of function and are among the most **disabling** and **costly** conditions in the United States

Overview



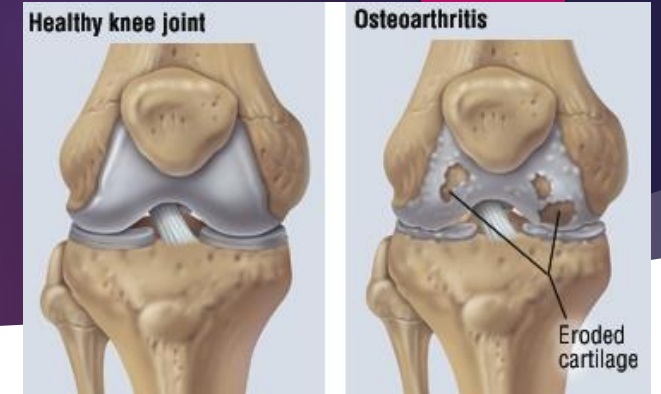
The Social Security Administration (SSA) defines disorders of the musculoskeletal system as conditions that might result from **hereditary, congenital, or acquired pathologic processes**. Impairments may result from infectious, inflammatory, or degenerative processes; traumatic or developmental events; or neoplastic, vascular, or toxic/metabolic diseases

Overview

In 2016 the top causes of years lived with disability in the United States included **low back pain (no. 1)**, other **musculoskeletal disorders (no. 4)**, **neck pain (no. 6)**, **OA (no. 12)**, and **RA (no. 20)**.



Overview

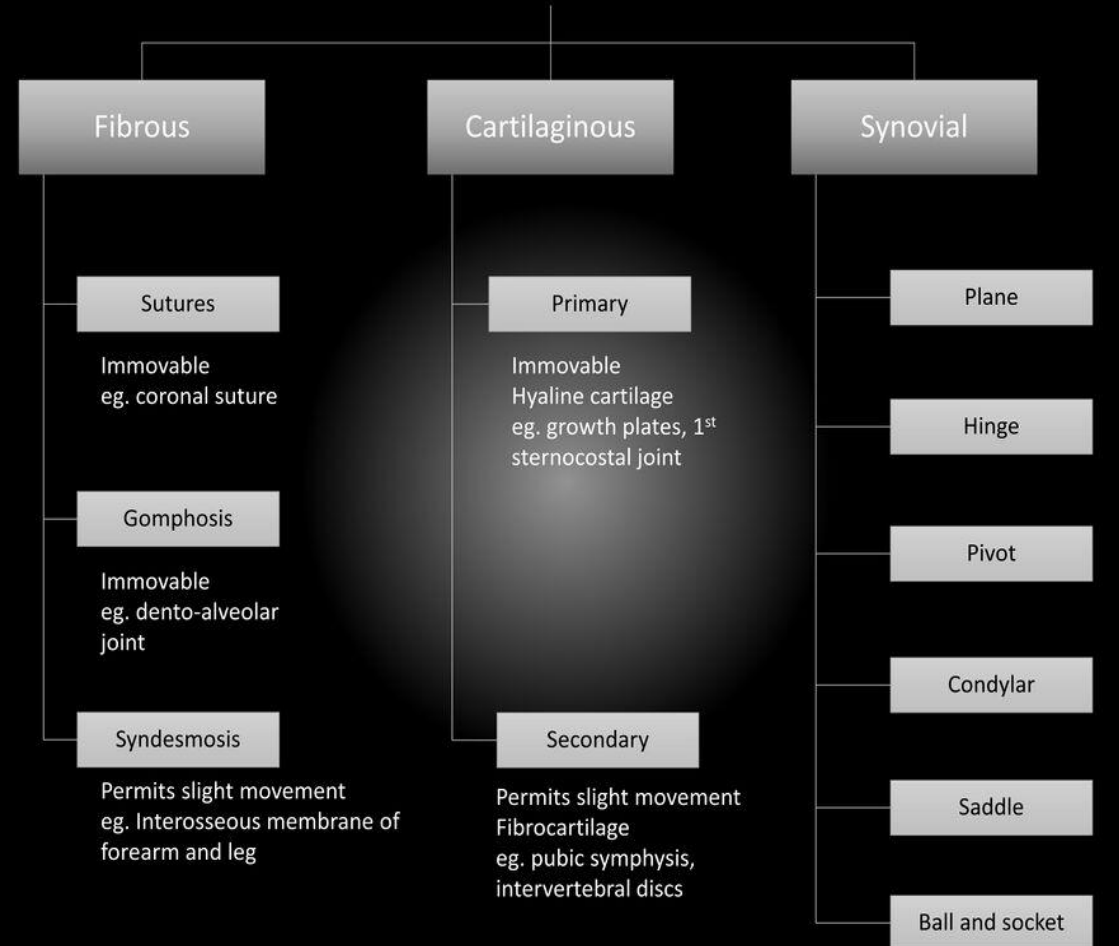


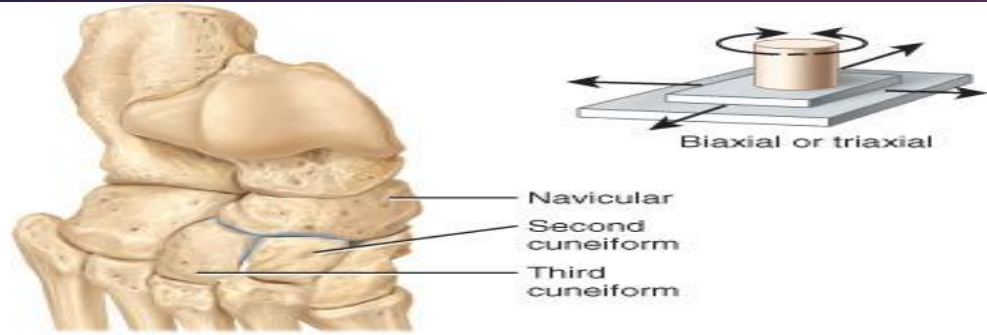
- ▶ the human body is composed of **206 bones**. At the point of contact between two or more bones an articulation (joint) is formed.
- ▶ There are two basic types of joints:
 - **synovial joints**: allow considerable movement (e.g. shoulder or knee)
 - **fibro cartilaginous joints**: are completely immovable (e.g. the skull) or permit only limited motion (e.g. spinal vertebrae).

Overview

- ▶ the human body is composed of 206 bones
- ▶ Joints can be classified:
 - ▶ Histologically, on the dominant type of connective tissue. ie **fibrous**, **cartilaginous**, and **synovial**.
 - ▶ Functionally, based on the amount of movement permitted. ie synarthrosis (immovable), amphiarthrosis (slightly moveable), and diarthrosis (freely moveable).

Structural classification of joints





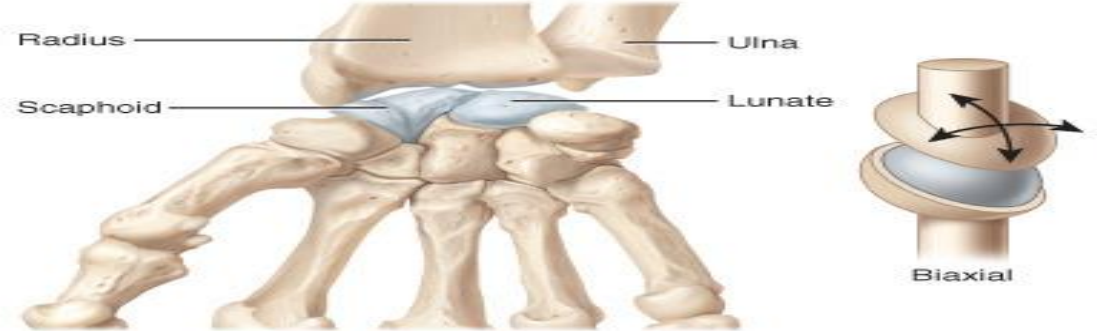
(a) Saddle joint between navicular and second and third cuneiforms of tarsus in foot



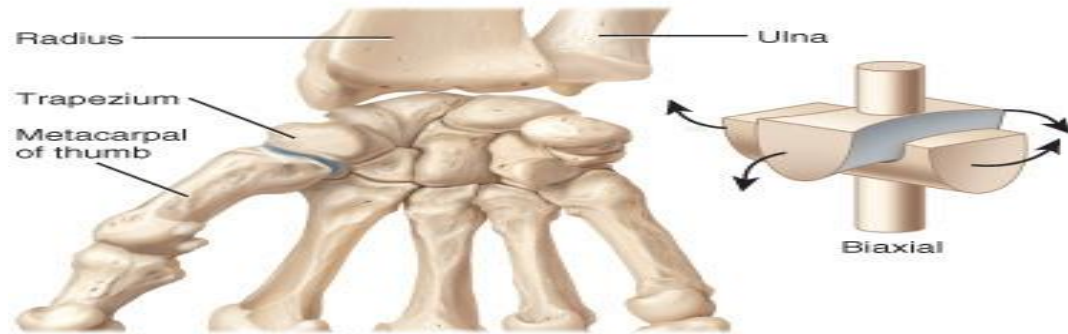
(b) Trochlear joint between trochlea of humerus and trochlear notch of ulna at the elbow



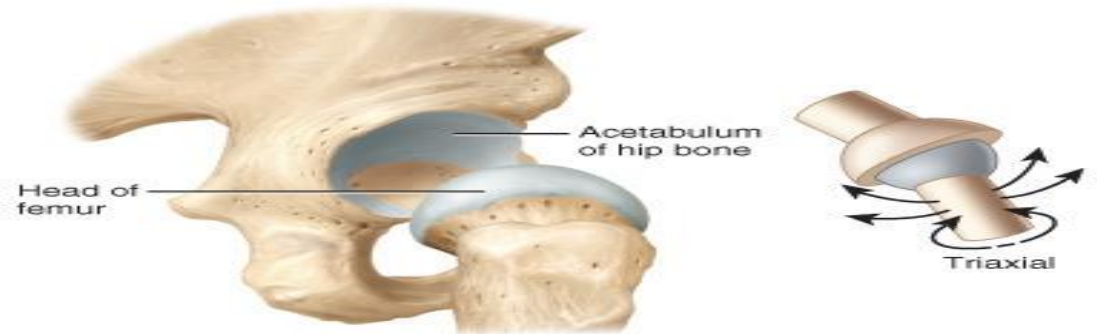
(c) Pivot joint between head of radius and radial notch of ulna



(d) Ellipsoidal joint between radius and scaphoid and ulna and lunate bones of carpus (wrist)



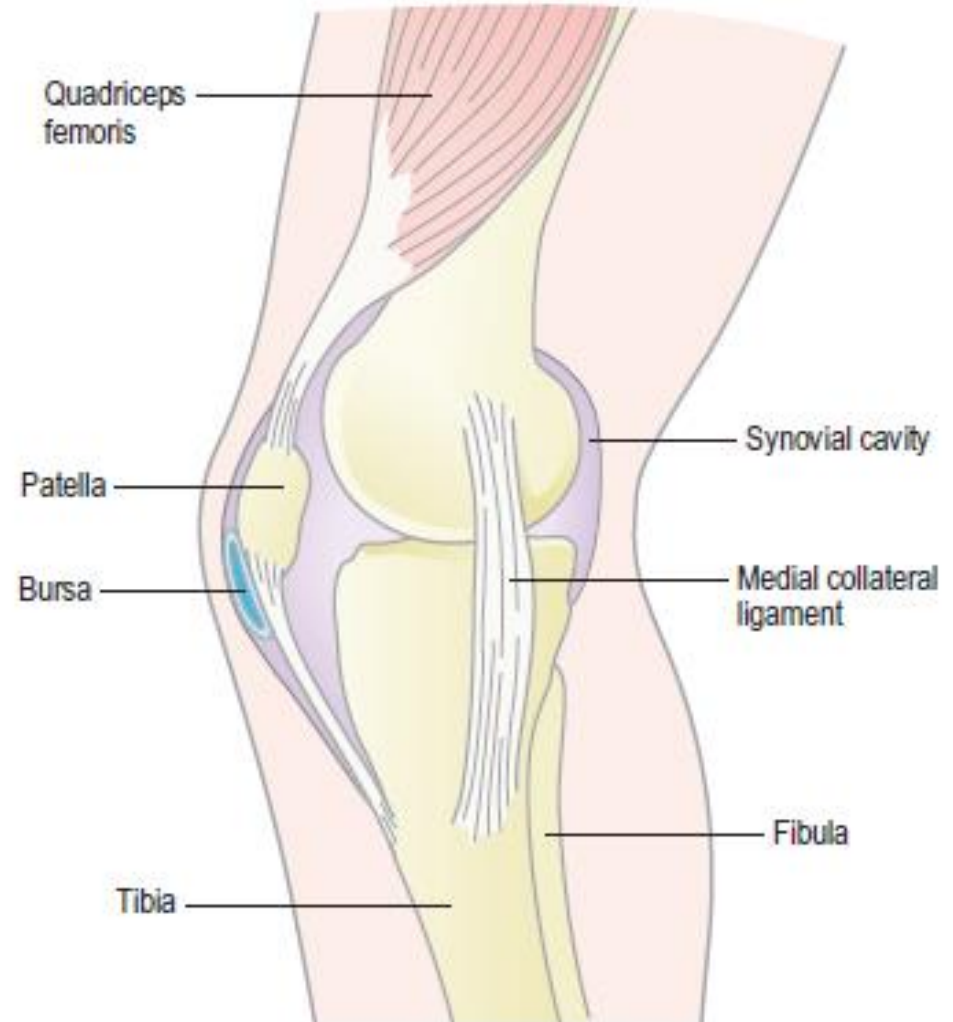
(e) Saddle joint between trapezium of carpus (wrist) and metacarpal of thumb



(f) Ball-and-socket joint between head of femur and acetabulum of hip bone

overview

The integrity of the musculoskeletal system depends on the interaction between skeletal muscle and bones, and coordinated movement is only possible because of the way muscle is attached to the bone.



overview

- ▶ Pain is One of the most common causes of seeking help from medical professionals.
- ▶ More than 2 Billion \$ spent per year in USA on nonprescription pain remedies.
- ▶ 80% of adults take pain medication at least once a week.
- ▶ musculoskeletal pain problems is estimated to burden the U.S economy over 60 billion \$ annually.

Osteoarthritis (OA)

- ▶ Osteoarthritis (OA) is the most common form of arthritis and possesses marked variability of disease expression. Although most patients present with joint pain and functional limitations, the **age of disease onset**, **sequence of joint involvement**, and **disease progression** vary from person to person.

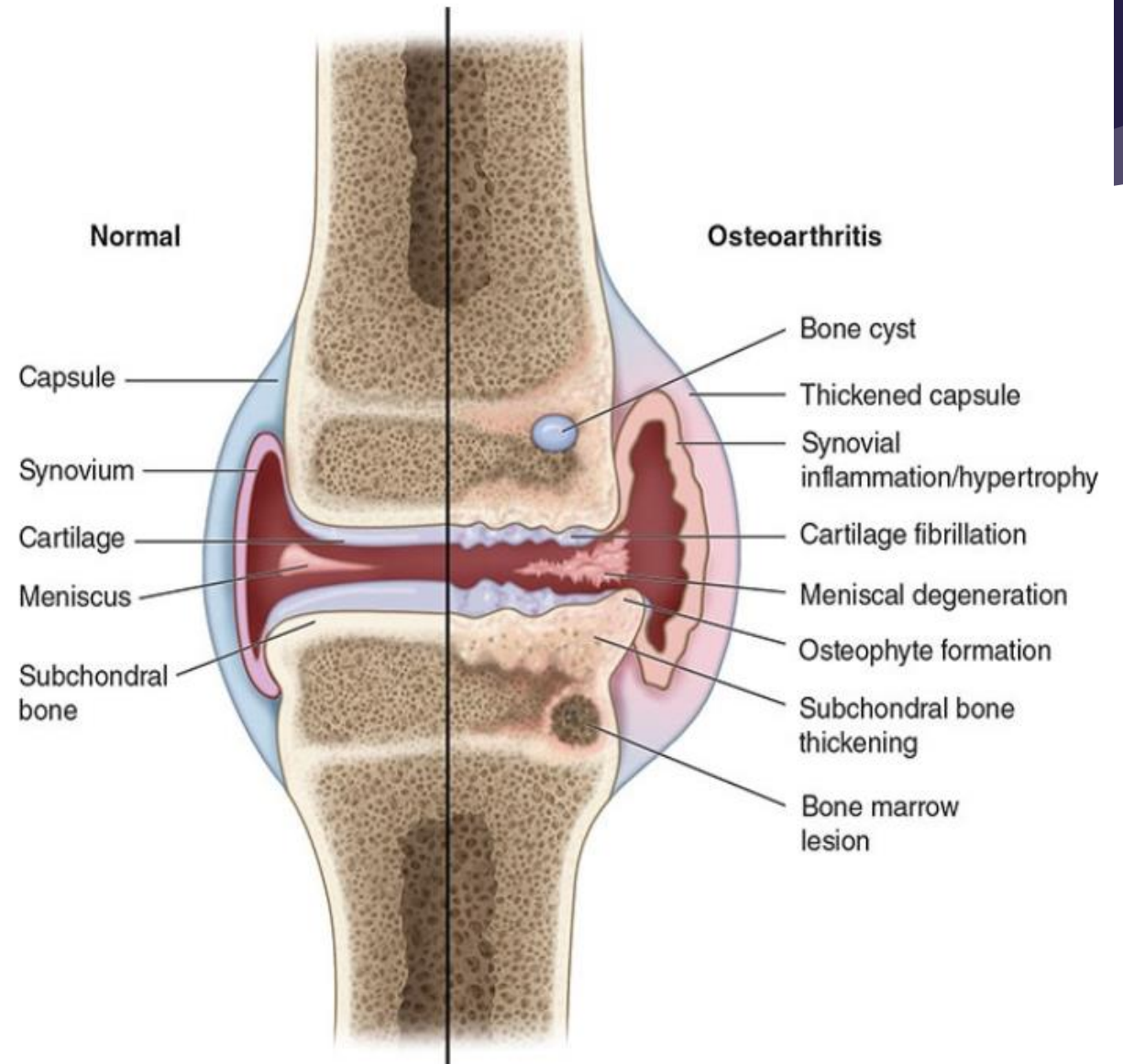
Osteoarthritis (OA)

- ▶ **Aging**
- ▶ **Gender**
- ▶ **Genetics**
- ▶ **Joint injury**
- ▶ **Anatomic factors**
- ▶ **Obesity**
- ▶ **Lifestyle factors**
- ▶ muscle weakness, smoking, bone density, and physical activity

RISK FACTORS

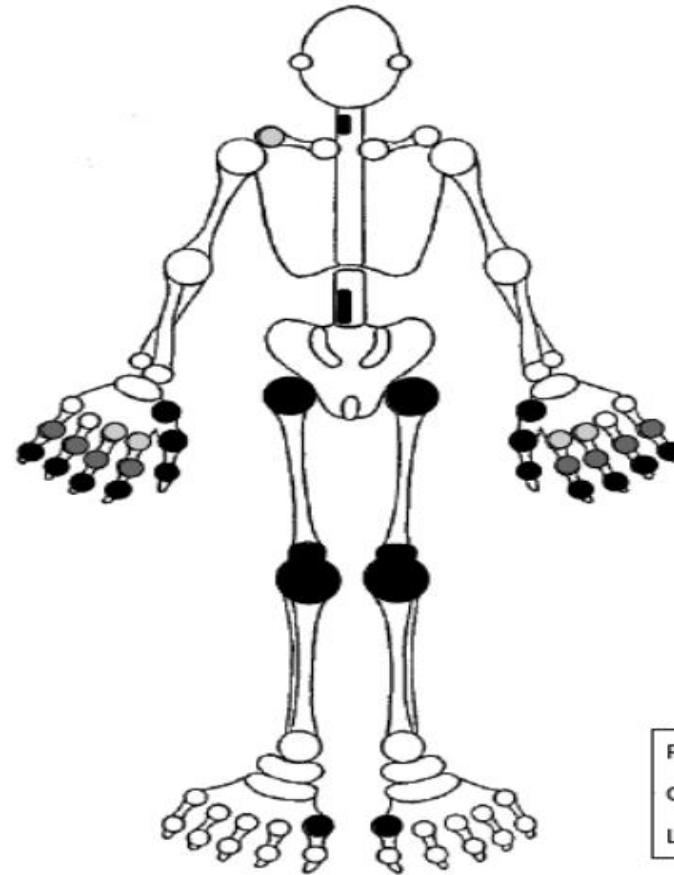


Osteoarthritis (OA)



Osteoarthritis (OA)

Joints affected in osteoarthritis



Target symptomatic joints for OA.

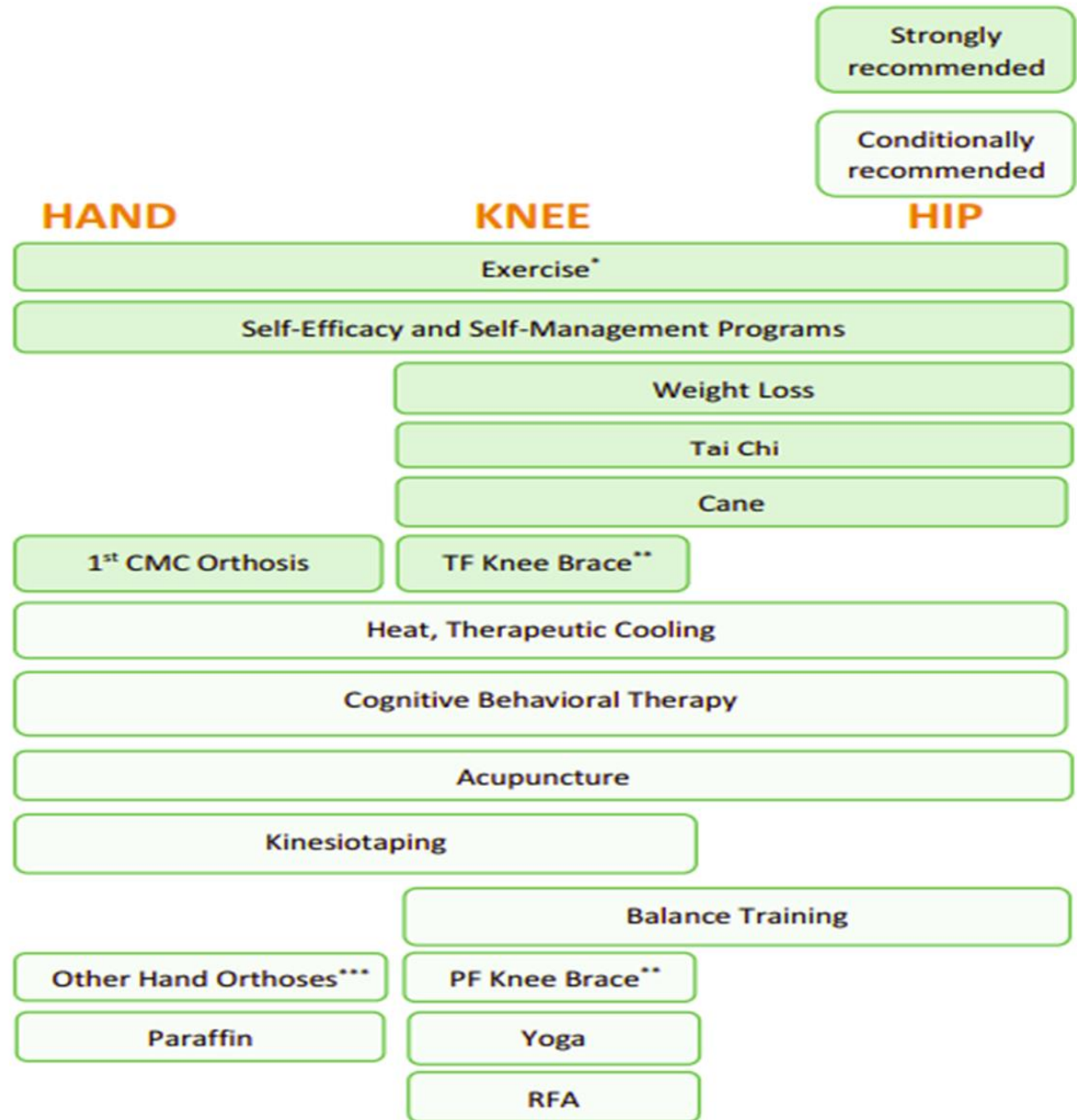
Osteoarthritis

Principal manifestations of osteoarthritis

Patient characteristics	
Age of onset	<ul style="list-style-type: none"> ■ >40 years*
Symptoms	
Pain	<ul style="list-style-type: none"> ■ Affects one or a few joints at a time ■ Insidious onset - slow progression over years ■ Variable intensity ■ May be intermittent ■ Increased by joint use and relieved by rest ■ Night pain in severe osteoarthritis
Stiffness	<ul style="list-style-type: none"> ■ Short-lived (<30 minutes) and early morning- or inactivity-related
Swelling	<ul style="list-style-type: none"> ■ Some (eg, nodal osteoarthritis) patients present with swelling and/or deformity
Constitutional symptoms	<ul style="list-style-type: none"> ■ Absent
Physical exam findings	
Appearance	<ul style="list-style-type: none"> ■ Swelling (bony overgrowth ± fluid/synovial hypertrophy) ■ Attitude ■ Deformity ■ Muscle wasting (global - all muscles acting over the joint)
Palpation	<ul style="list-style-type: none"> ■ Absence of warmth ■ Swelling (effusion if present is usually small and cool) ■ Joint line tenderness ■ Periarticular tenderness (especially knee, hip)
Range of motion	<ul style="list-style-type: none"> ■ Crepitus (knee, thumb bases) ■ Reduced range of movement ■ Weak local muscles

Osteoarthritis ACR 2019

PHYSICAL, PSYCHOSOCIAL, and MIND-BODY APPROACHES



Strongly recommended

Conditionally recommended

Osteoarthritis(OA)

ACR 2019

PHARMACOLOGIC APPROACHES

Oral NSAIDs

Topical NSAIDs

Topical NSAIDs

I-A Steroids

I-A Steroids (Imaging-Guidance for Hip)

Acetaminophen

Tramadol

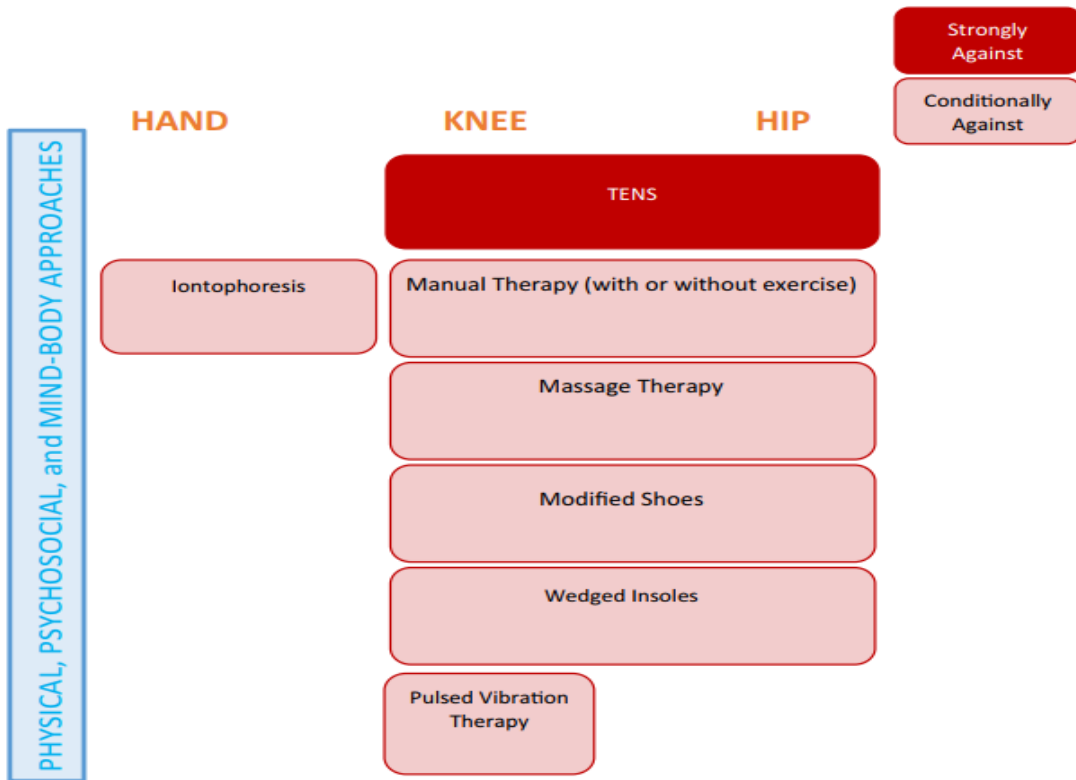
Duloxetine

Chondroitin

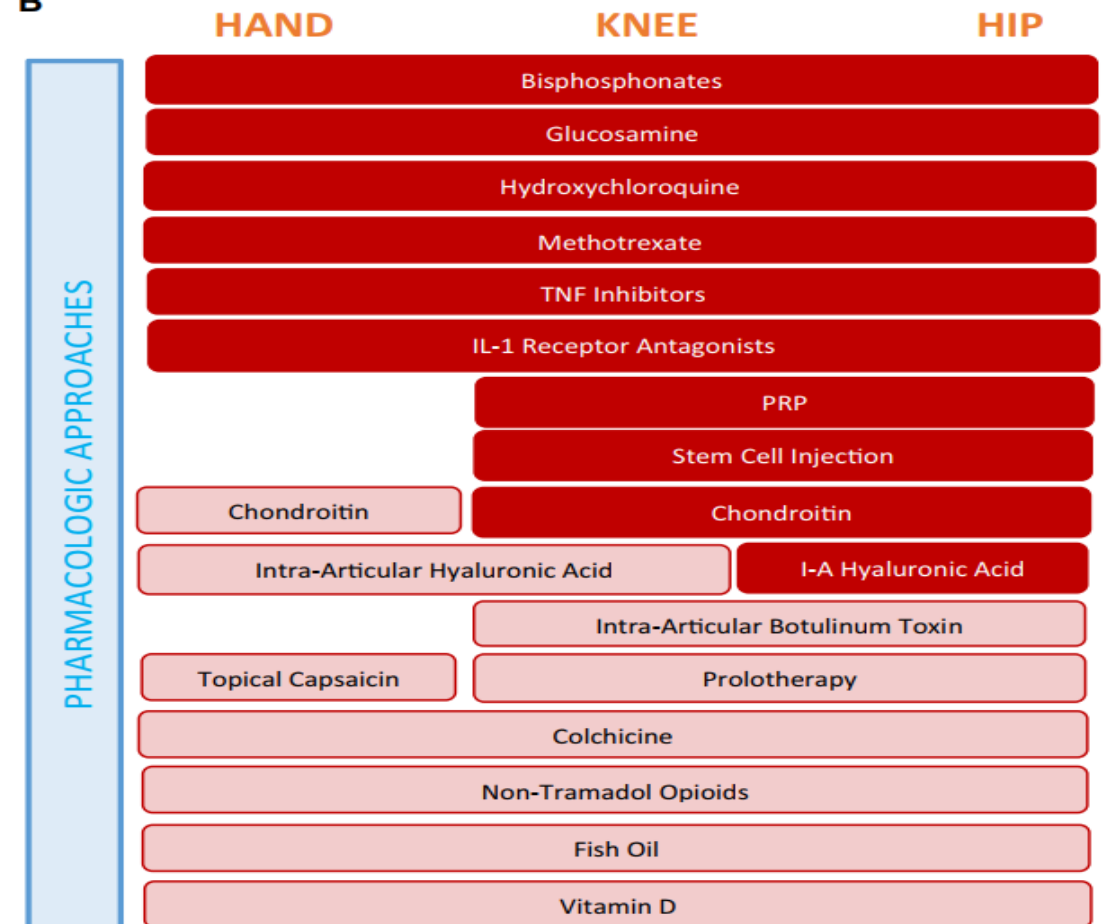
Topical Capsaicin

Osteoarthritis (OA) ACR 2019

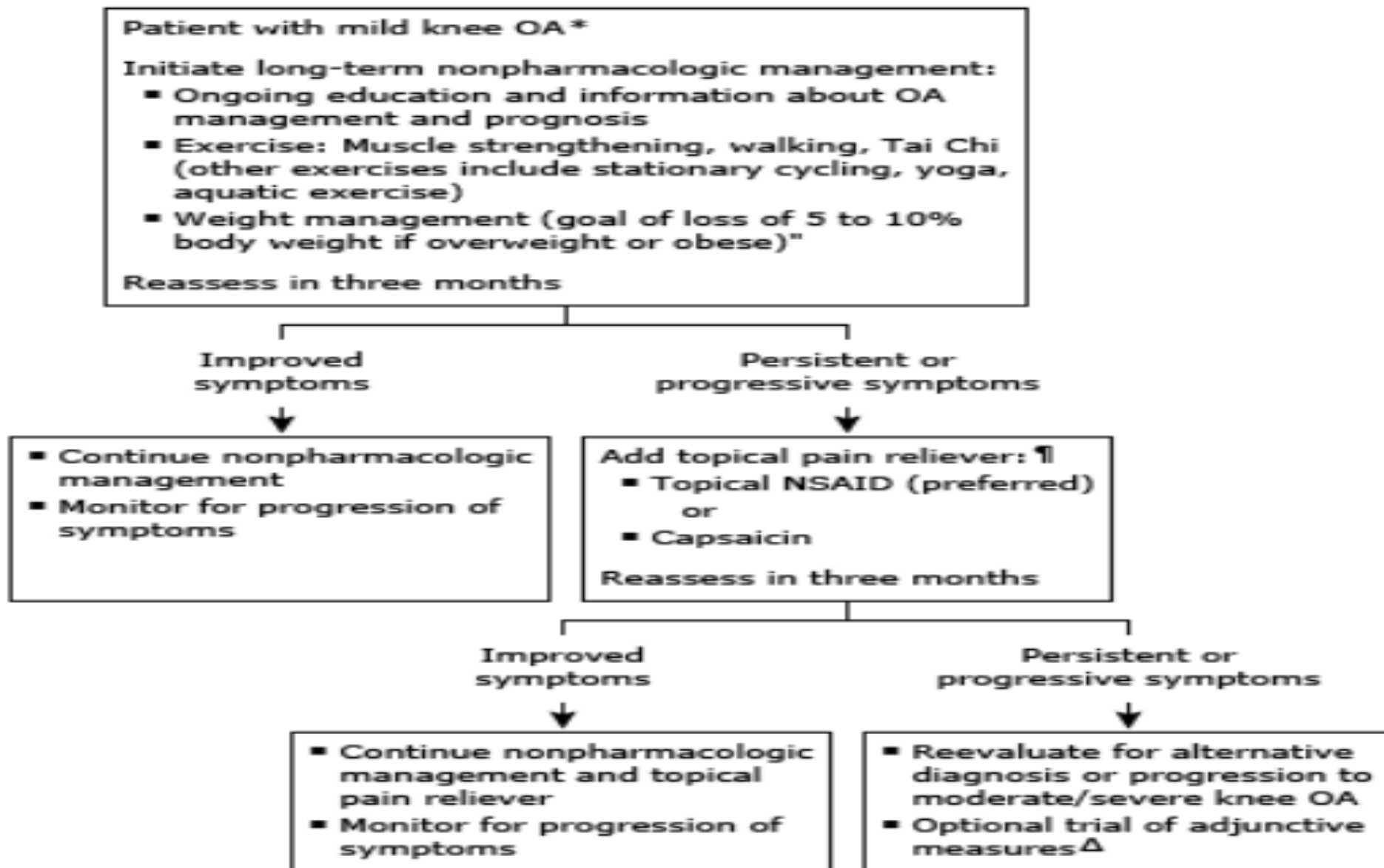
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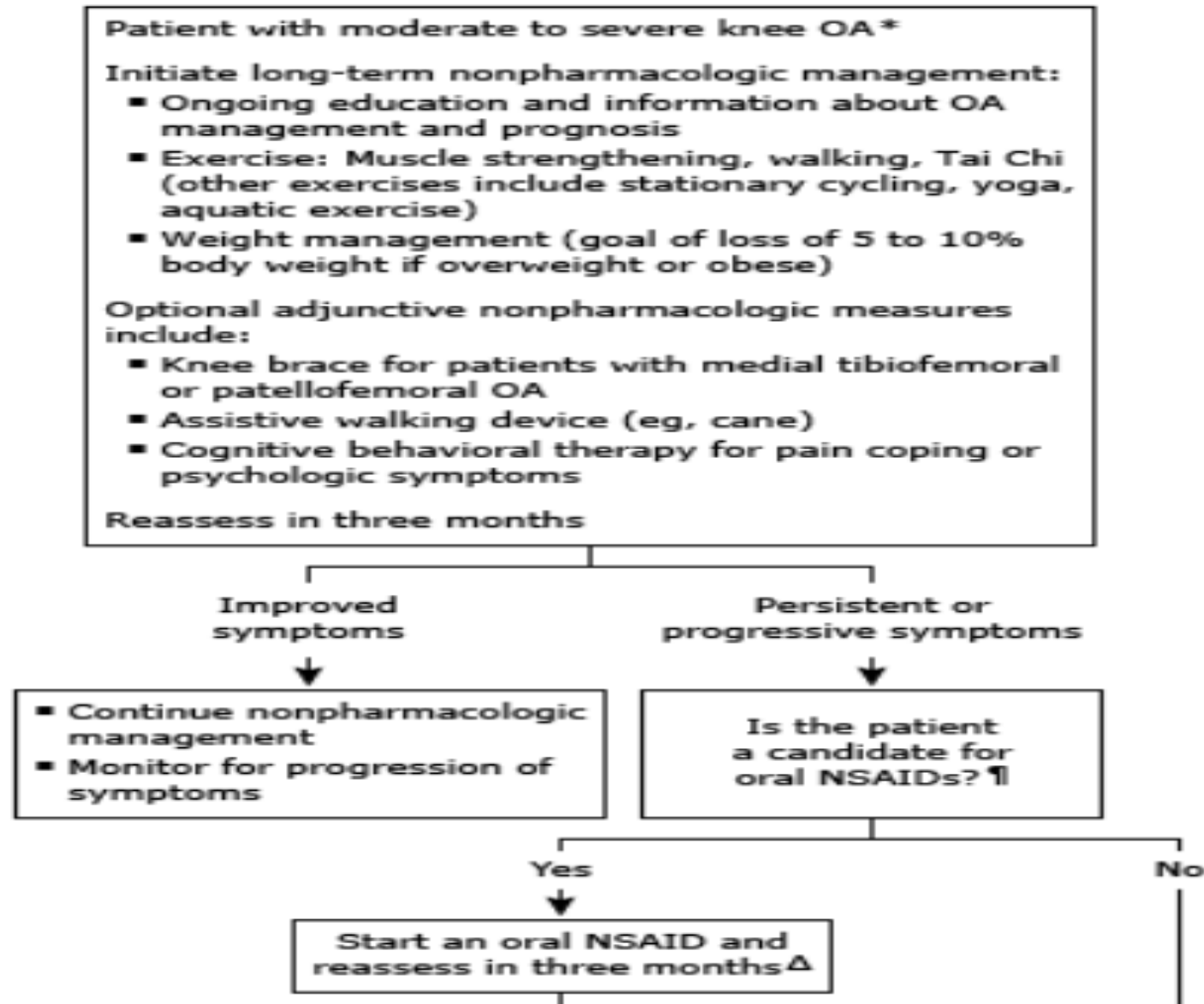
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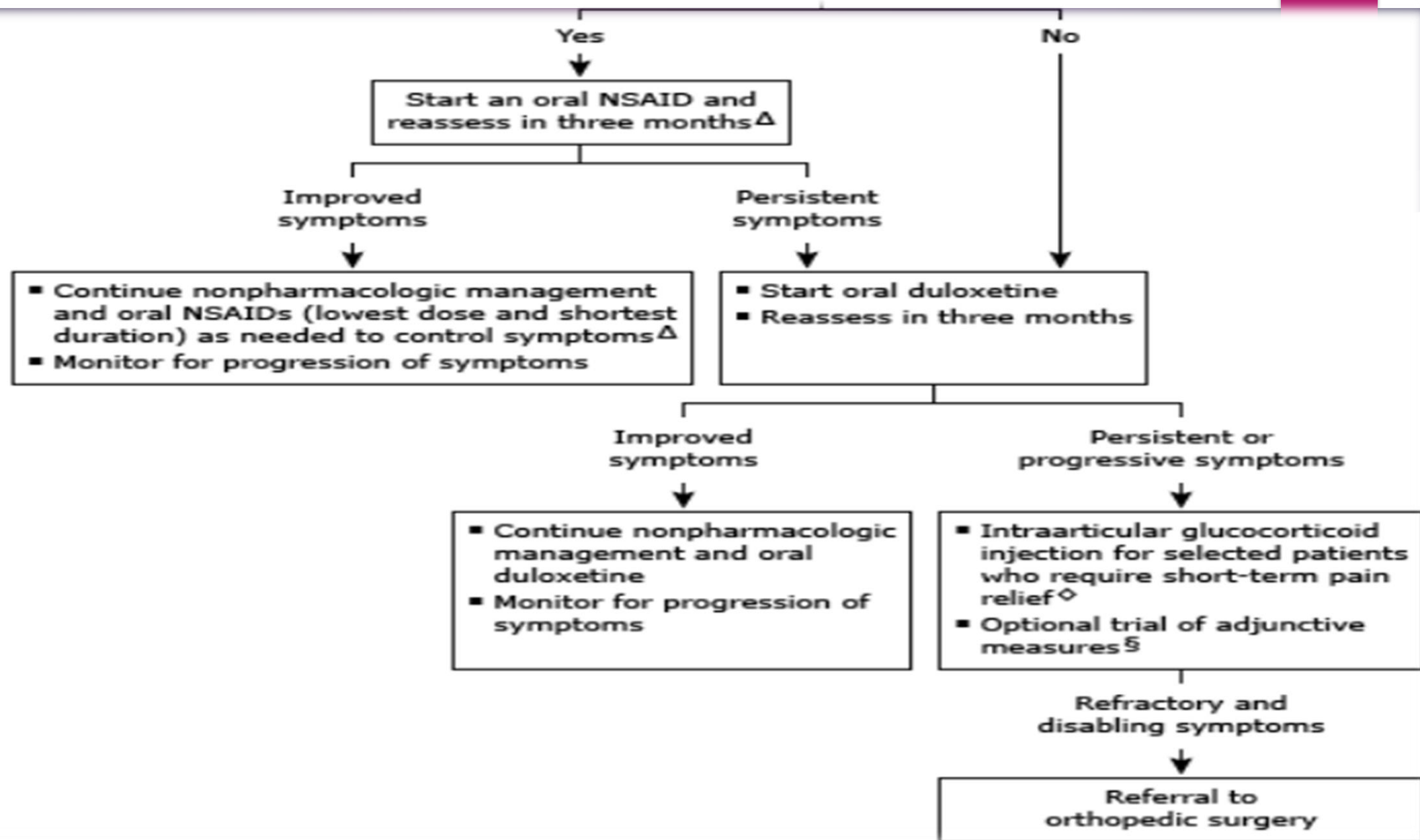


Management of mild knee osteoarthritis



Management of moderate to severe knee osteoarthritis





Topical analgesics for treatment of knee and hand osteoarthritis

Topical analgesic	Usual dose (adult)
Topical nonsteroidal antiinflammatory drugs (NSAIDs)*	
Diclofenac topical gel (1%)	Knees: rub in 4 g of gel to affected knee(s) three to four times daily Hands: rub in 2 g of gel to affected joint(s) three to four times daily Maximum 16 g per joint per day; 32 g total per day
Diclofenac topical solution drops (1.5%)	Knees: rub in 40 drops to affected knee(s) up to four times daily
Diclofenac topical solution pump (2%)	Knees: rub in two pump actions to affected knee(s) up to two times daily
Ibuprofen topical gel (5, 10%); not available in the United States	Knees or hands: rub in dose (depends on joint size and location) up to four times daily; refer to product-specific information for detail
Ketoprofen topical gel (2.5%); not available in the United States	Knees or hands: rub in 2 to 4 g of gel two to four times daily (maximum 15 g of gel per day); refer to product-specific information for detail
Topical capsaicin[¶]	
Capsaicin creams, gels, liquids, lotions (0.025 to 0.1%)	Rub in a small amount (pea-sized) one to four times daily; the preparation most often studied in osteoarthritis was 0.025% cream
Capsaicin topical patches (0.025 to 0.05%)	Apply one patch to affected area for up to eight hours (maximum four patches per day)

Topical NSAIDs



?

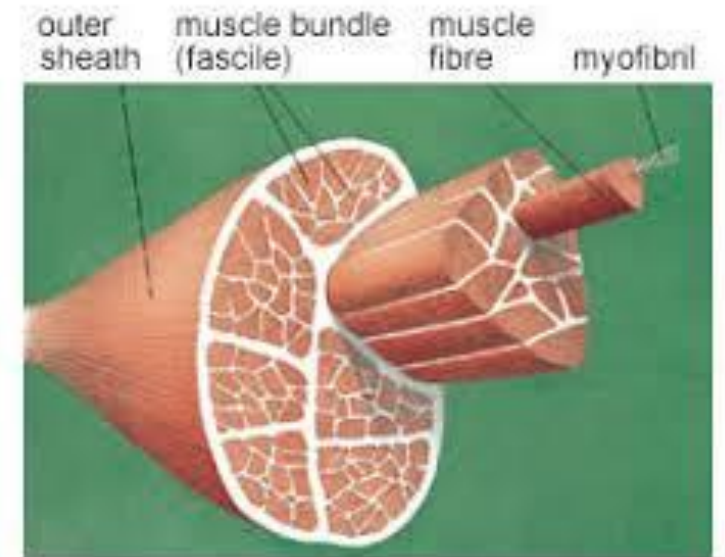


It is also widely used for livestock; such use was responsible for the Indian vulture crisis, during which in a few years 95% of the country's vulture population was killed, and in many countries agricultural use is now forbidden

Myalgia

Myalgia is the medical term for **muscle pain**. Muscle pain is a symptom of many diseases and conditions. Myalgia can be acute (short-term) or chronic (long-term).

With chronic myalgia, however, muscle pain hurts with both rest and movement. Muscles can also be tender and swollen. Muscle pain is the hallmark symptom of some chronic conditions like **fibromyalgia**.



Myalgia

- ▶ Muscle pain can be **localized** to one muscle group or **diffuse**, involving multiple muscle groups. Muscle pain due to injury or overuse is most commonly localized to one area. Depending upon the cause, muscle pain can be **mild** or **severe and debilitating**

Myalgia

- ▶ Infection:
 - ❑ Viral
 - ❑ Bacterial
- ▶ Chronic disease:
 - ❑ Fibromyalgia
 - ❑ Polymyalgia rheumatica
- ▶ Medications:
 - ❑ Statins
- ▶ Dietary factors:
 - ❑ Alcoholism
 - ❑ Vitamin D deficiencies



Myalgia



- ▶ Water retention or decreased urine output
- ▶ Problems swallowing
- ▶ Trouble breathing or catching your breath
- ▶ Neck stiffness
- ▶ Weak muscles
- ▶ Inability to move the affected area, or paralysis

Fibromyalgia

Fibromyalgia is a disorder characterized by **widespread musculoskeletal pain** accompanied by **fatigue, sleep, memory** and **mood issues**. Researchers believe that fibromyalgia amplifies painful sensations by affecting the way your brain and spinal cord process painful and no painful signals.



Fibromyalgia



Fibromyalgia

Symptoms often begin after an event, such as physical trauma, surgery, infection or significant psychological stress. In other cases, symptoms gradually accumulate over time with no single triggering event.

Women are more likely to develop fibromyalgia than men. Many people who have fibromyalgia also have **tension headaches**, **IBS**, **anxiety** and **depression**.

Fibromyalgia- Diagnostic Criteria

Criteria

A patient satisfies diagnostic criteria for fibromyalgia (FM) if the following three conditions are met:

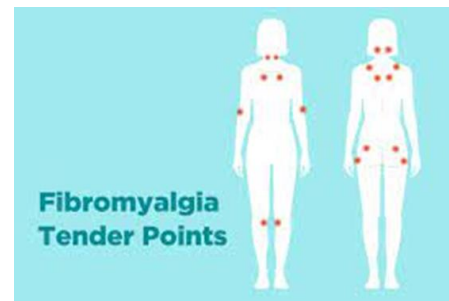
1. WPI ≥ 7 and SSS ≥ 5 OR WPI of 4-6 and SSS ≥ 9
2. Generalized pain, defined as pain in at least 4 of 5 regions, must be present. **Jaw, chest, and abdominal pain are not included in generalized pain definition.**
3. Symptoms have been generally present for at least 3 months. A diagnosis of FM is valid irrespective of other diagnoses. A diagnosis of FM does not exclude the presence of other clinically important illnesses.

Widespread Pain Index (WPI)
(1 point per check box; score range: 1-19)

Please check the boxes below for each area in which you have had pain or tenderness **during the past 7 days**.

<input type="checkbox"/> Shoulder girdle, left	<input type="checkbox"/> Lower leg left
<input type="checkbox"/> Shoulder girdle, right	<input type="checkbox"/> Lower leg right
<input type="checkbox"/> Upper arm, left	<input type="checkbox"/> Jaw left
<input type="checkbox"/> Upper arm, right	<input type="checkbox"/> Jaw right
<input type="checkbox"/> Lower arm, left	<input type="checkbox"/> Chest
<input type="checkbox"/> Lower arm, right	<input type="checkbox"/> Abdomen
<input type="checkbox"/> Hip (buttock) left	<input type="checkbox"/> Neck
<input type="checkbox"/> Hip (buttock) right	<input type="checkbox"/> Upper back
<input type="checkbox"/> Upper leg left	<input type="checkbox"/> Lower back
<input type="checkbox"/> Upper leg right	<input type="checkbox"/> None of these areas

WPI score: _____



Symptom severity scale (SSS) score:

Fatigue

Waking unrefreshed

Cognitive symptoms

Headaches

Pain or cramps in lower abdomen

Depression

Fibromyalgia- Diagnoses

Chronic (>3 months) widespread musculoskeletal pain

History

- Personal or family history of pain
- Pain quality and anatomic location
- Associated symptoms of fatigue, unrefreshing sleep, dyscognition, depression/anxiety, perceived stress
- Medications

Physical examination

- Tenderness assessment
- Musculoskeletal examination for synovitis, degenerative change, soft tissue disorders (bursitis, tendonitis), hypermobility
- Connective tissue features such as rash, mucositis, Raynaud's phenomenon
- Neurologic examination

Testing

- CBC, metabolic panel
- ESR or CRP
- TSH
- Vitamin D
- Other testing guided by H&P

Determine category

FM

- Meets ACR criteria
- Physical examination normal except widespread allodynia
- Laboratory testing normal
- No suspicious medications

Initiate FM treatment

- Educate patient
- Determine symptom domain(s) for initial treatment focus
- Implement nonpharmacologic program of exercise and behavioral management
- Begin pharmacologic treatment according to primary symptom profile
 - Pain/sleep: TCA, gabapentinoid
 - Fatigue/depression: NSRI

Comorbid FM

- Other condition contributing to overall clinical picture, but may not explain entire symptom complex
- Meets 1990 ACR criteria¹⁵

Treat comorbid disorder and nonpharmacologic FM treatment

- Initiate treatment of primary disorder
- Educate patient about FM
- Add exercise program, depression/anxiety treatment, and/or sleep management program if clinically appropriate
- Assess need for pharmacologic treatment of FM once primary disorder treated

Not FM

- Alternative diagnosis is likely to explain clinical findings
- Does not meet ACR criteria

Treat alternative disorder

- Consider re-evaluation for FM if widespread pain persists despite adequate treatment of alternative disorder

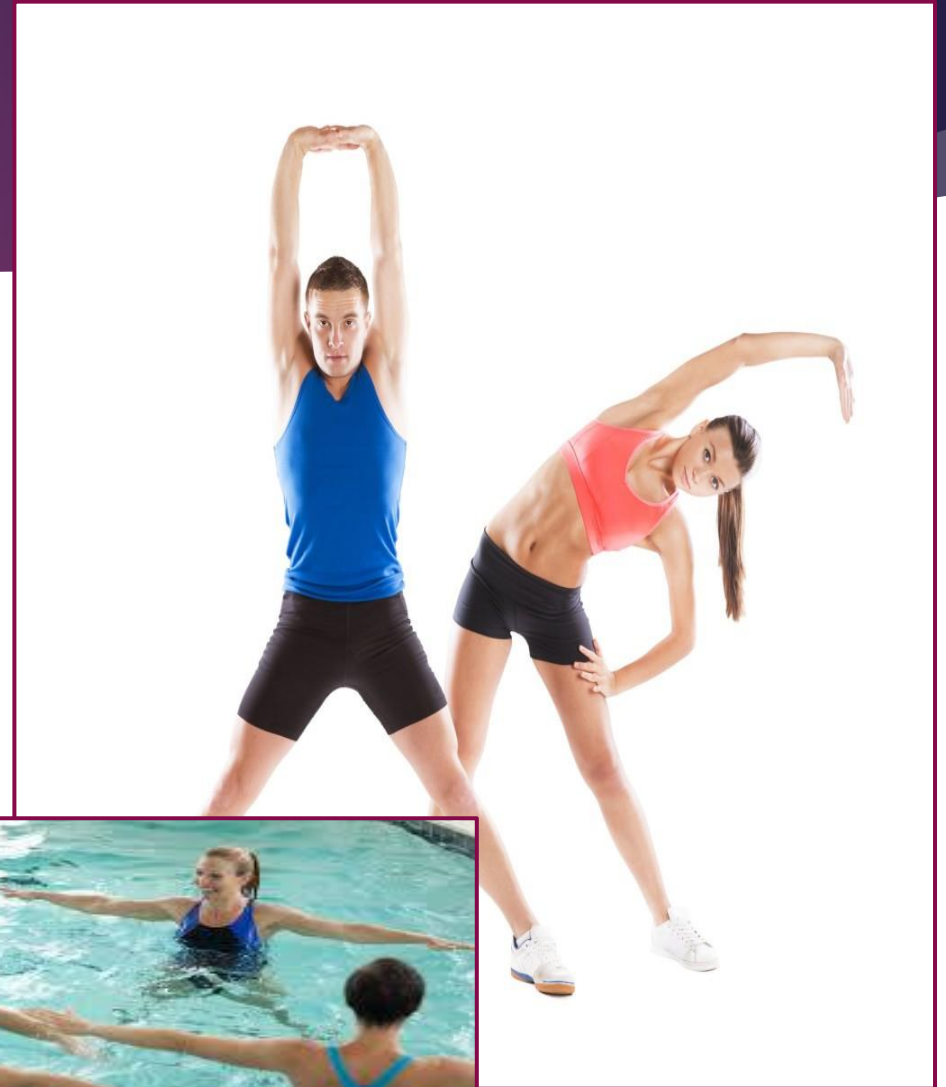
Fibromyalgia- treatment

- ▶ While there is no cure for fibromyalgia, a variety of medications can help control symptoms. **Exercise, relaxation** and **stress-reduction** measures also may help.



Fibromyalgia- treatment

The variability of the interventions did not allow for recommendations regarding the mode of exercise or the frequency, intensity, and duration of treatments.



Drug induced myopathy

Direct myotoxicity

- alcohol
- glucocorticoids

Immunologically induced inflammatory myopathy

- D-penicillamines
- statins

Indirect muscle damage

- phenothiazines
- cocaine



Spectrum of statin-associated muscle adverse events

Term	Clinical findings	Histopathological findings ^[1]
Myalgia	<p>Unexplained muscle discomfort often described as "flu-like" symptoms with normal CK level</p> <p>The spectrum of myalgia complaints includes:</p> <ul style="list-style-type: none"> ▪ Muscle aches; ▪ Muscle soreness; ▪ Muscle stiffness; ▪ Muscle tenderness; and ▪ Muscle cramps with or shortly after exercise (not nocturnal cramping) 	None
Myopathy	Muscle weakness (not attributed to pain and not necessarily associated with elevated CK)	Variable findings: <ul style="list-style-type: none"> ▪ Atrophy ▪ Inflammation ▪ Mitochondrial changes
Myositis	Muscle inflammation	T cells > B cells; macrophages
Myonecrosis	Muscle enzyme elevations or hyperCKemia <ul style="list-style-type: none"> ▪ Mild: >3-fold greater than baseline untreated CK levels or normative upper limit that are adjusted for age, race, and sex ▪ Moderate: ≥10-fold greater than untreated baseline CK levels or normative upper limit that are adjusted for age, race, and sex ▪ Severe: ≥50-fold above baseline CK levels or normative upper limit that are adjusted for age, race, and sex 	Non-specific inflammatory cells with secondary macrophage infiltration
Myonecrosis with myoglobinuria (rhabdomyolysis)	Increase in serum creatinine ≥0.5 mg/dL (clinical rhabdomyolysis)	Non-specific inflammatory cells with secondary macrophage infiltration

Myalgia

To ease muscle pain due to overuse or injury, rest the body part and take acetaminophen or ibuprofen. **Applied ice within the first 24 to 72 hours of an injury can reduce pain and inflammation. After that, heat can be more soothing.** Muscle pain from overuse and fibromyalgia respond well to massage and gentle stretching exercises.

muscle cramp

- ▶ A muscle cramp is a **sudden** and **involuntary contraction** of one or more of your muscles
- ▶ cause severe pain
- ▶ generally harmless
- ▶ Some medications and certain medical conditions



muscle cramp

Muscle Cramp Causes



Poor conditioning



Altered neuromuscular control



Doing a new activity



Muscle fatigue



Electrolyte depletion



Dehydration

muscle cramp



- ▶ Cause severe discomfort
- ▶ Are associated with leg swelling, redness or skin changes
- ▶ Are associated with muscle weakness
- ▶ Happen frequently
- ▶ Don't improve with self-care
- ▶ Aren't associated with an obvious cause, such as strenuous exercise

muscle strain

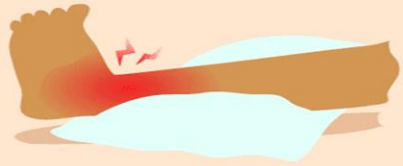
A muscle strain is the stretching or tearing of muscle fibers. Most muscle strains happen for one of two reasons: either the muscle has been stretched beyond its limits or it has been forced to contract too strongly.

- ▶ **Grade I strain**
- ▶ **Grade II strain**
- ▶ **Grade III strain**



muscle strain

R



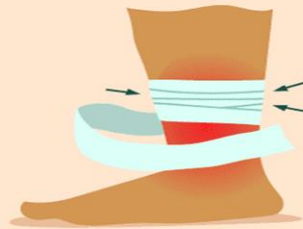
Rest
the injured
area for 48 hours

I



Ice
for 20 minutes
at a time,
4 to 8 times
per day

C



Compress
to help
reduce swelling

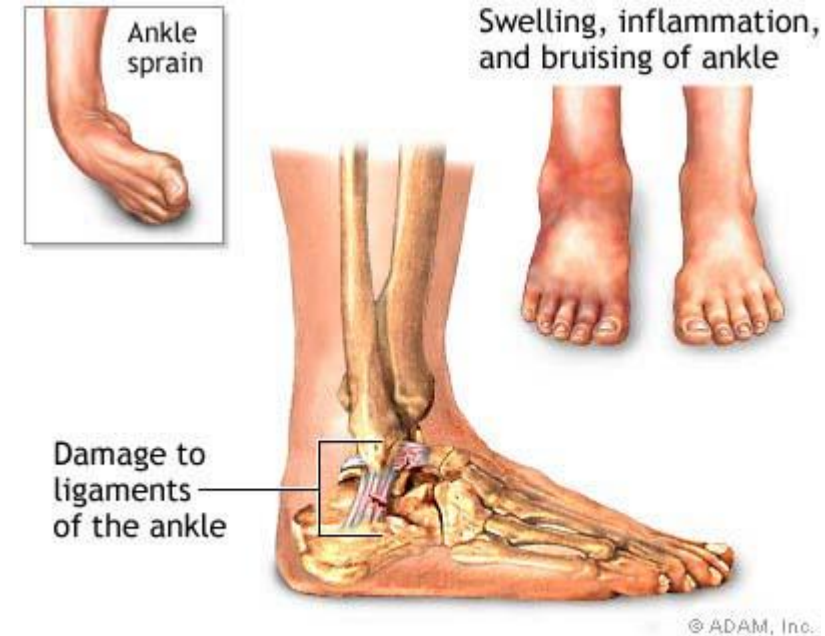
E



Elevate
the injured limb
6 to 10 inches
above the heart

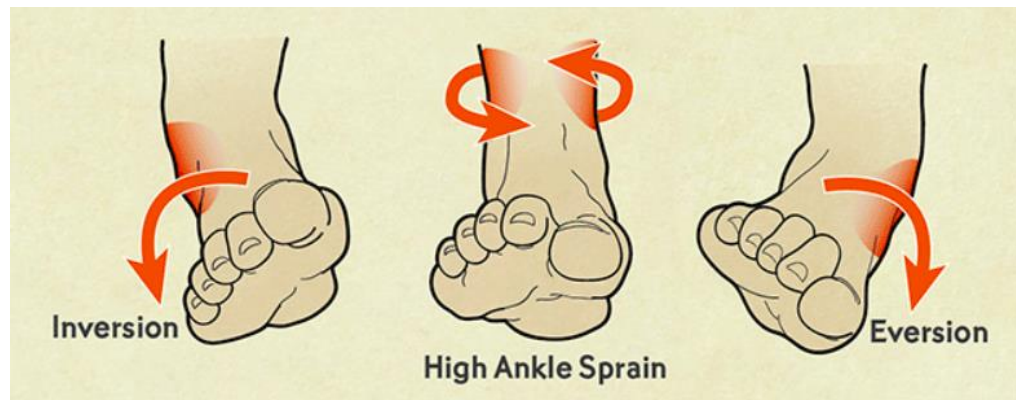
Sprain

A sprain, also known as a torn ligament, is damage to one or more ligaments in a joint, often caused by trauma or the joint being taken beyond its functional range of motion.



Sprain

When a joint is sprained, its torn or stretched ligaments can lose part or all of their ability to reinforce the joint and to keep it moving normally. In severe cases, the sprained joint can become unstable and loose, bones can move out of alignment and the joint may extend beyond its normal range of motion.



Sprain

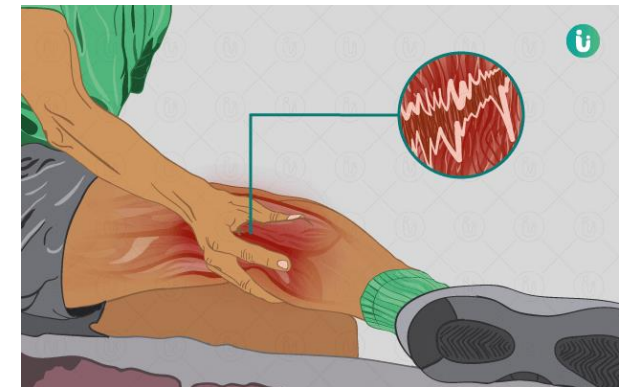


3 Degrees of Ankle Sprains

- Grade I: Mild degree of ankle sprain:** Slight tearing of the ligament with mild swelling.
- Grade II: Moderate degree of ankle sprain:** Incomplete tearing of the ligament with moderate pain and bruising.
- Grade III: Severe degree of ankle sprain:** Complete tearing of the ligament with severe swelling, pain, and bruising.

Strain vs sprain

The difference between a strain and a sprain is that a strain involves an injury to a muscle or to the band of tissue that attaches a muscle to a bone, while a sprain injures the bands of tissue that connect two bones together.



Strain vs strain



Strain and strain

- ▶ After 2 weeks, most sprains and strains will feel better.
- ▶ Avoid strenuous exercise such as running for up to 8 weeks, as there's a risk of further damage.
- ▶ Severe sprains and strains can take months to get back to normal.

Tendonitis

- ▶ Acute injury:
- ▶ Chronic overuse:

- Fluoroquinolones
 - >60yr old
 - Concomitant steroid
 - Transplant patients



Tendonitis



Bursitis

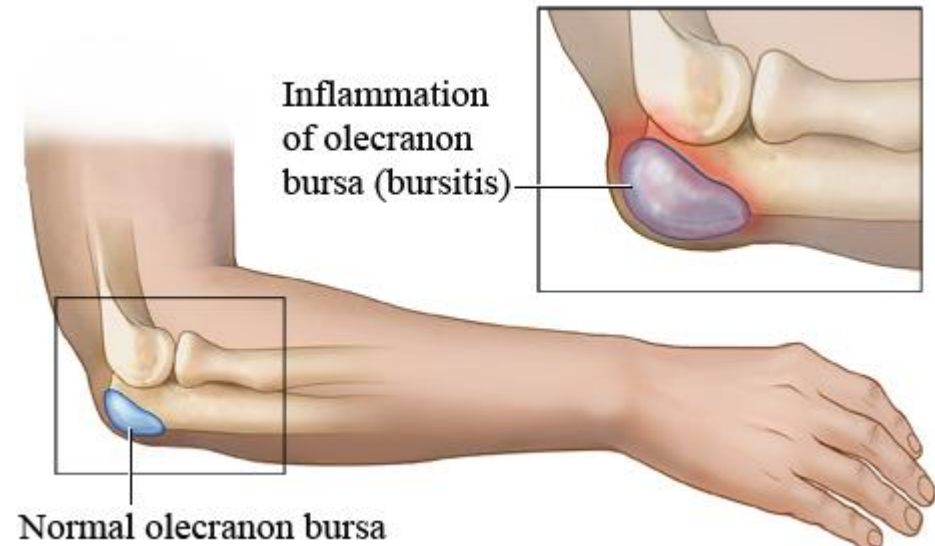
The inflammation of one or more bursae (small sacs) of synovial fluid in the body.

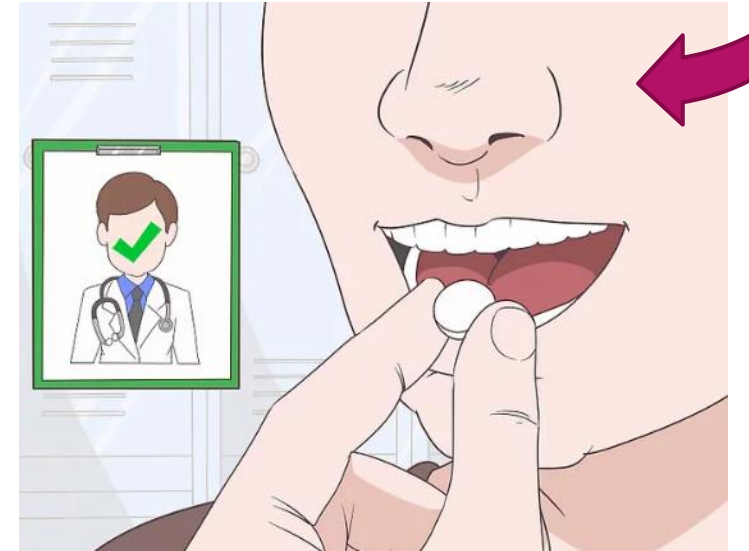
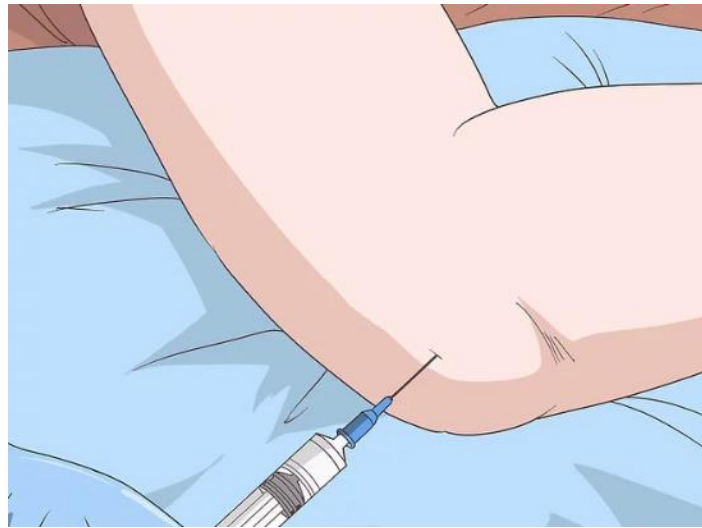
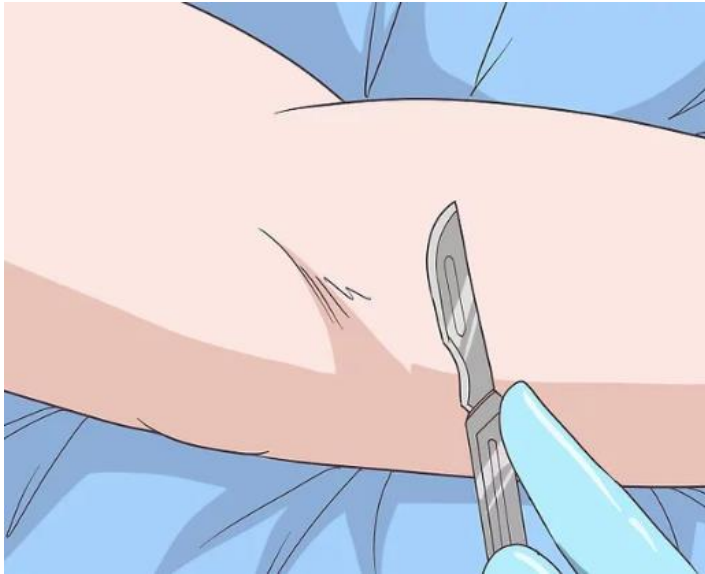
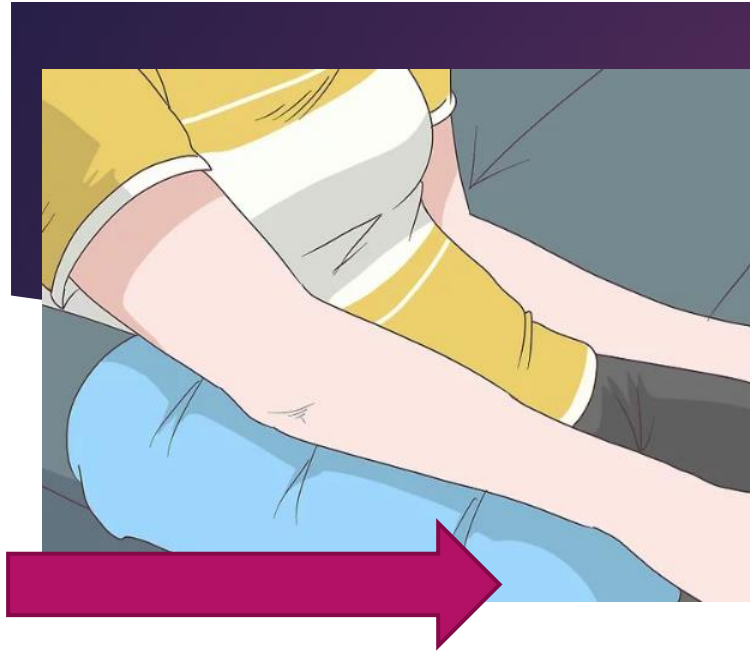
▶ Acute injury:

- ❑ Injection site
- ❑ Infection
- ❑ Inflammation

▶ Chronic injury:

- ❑ Repetitive task





Comparison of musculoskeletal disorders:

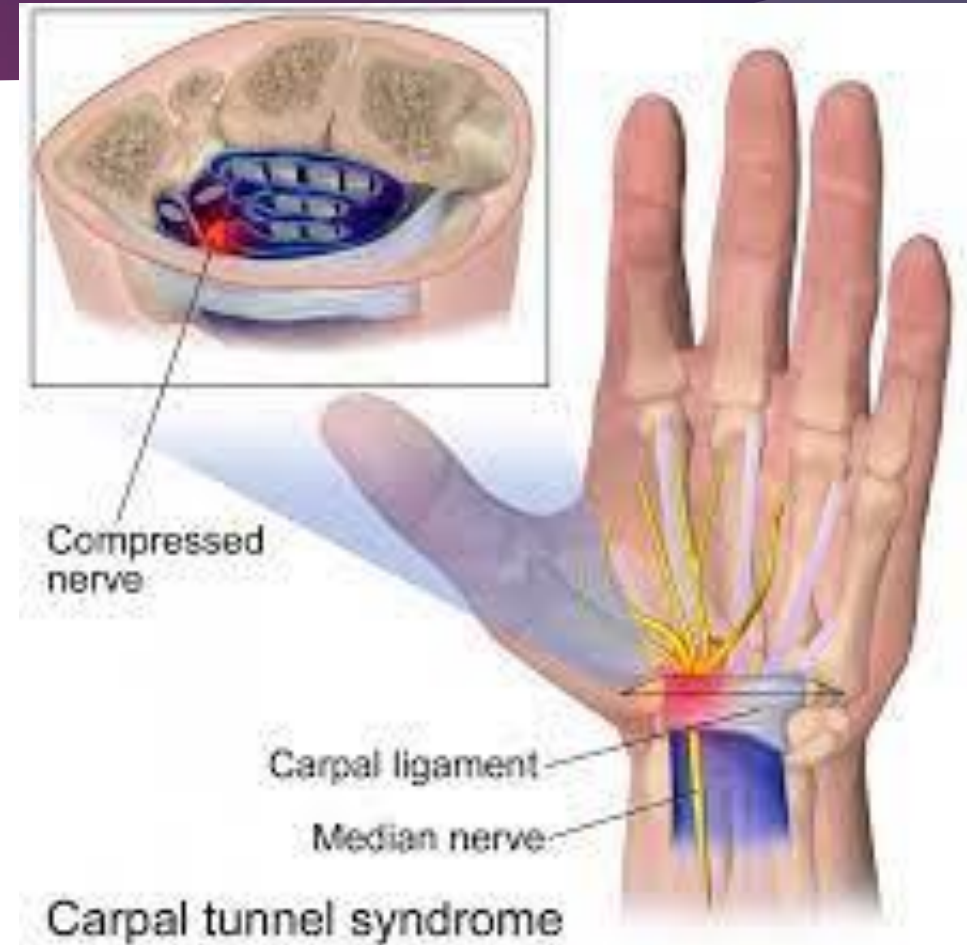
	Myalgia	Tendonitis	Bursitis	Sprain	strain	osteoarthritis
location	Muscles of body	Tendons around joints	Knee shoulder & toe	Ligaments within joints	Muscle or ligament	Weight bearing joints knees, hips, low back, hands
Signs	Swelling(rare)	Warmth swelling, erythema	Warmth swelling, erythema Crepitus	Swelling, bruising	Swelling, bruising	Deformity of joints, swelling
Symptoms	Dull constant ache, weakness fatigue	Mild to severe pain after use, Limited range of motion.	Constant pain that worsens with movement and pressure	Initial severe pain followed by pain with use reduction of joint movement	Initial severe pain followed by pain with use muscle weakness, loss of function	Dull pain relived by rest, stiffness, localized to joint.

Comparison of musculoskeletal disorders:

	Myalgia	Tendonitis	Bursitis	Sprain	strain	osteoarthritis
Onset	Dependent on cause	Gradual, sudden	Acute with injury worsen with use	Acute with injury	Acute with injury	Insidious over years
Exacerbating factor	Contraction	Movement	Movement	Movement	Use of muscle	Obesity, sedentary life, heavy activity, repetitive task trauma
Modifying factor	Elimination of cause, stretching, rest, heat, systemic or topical analgesics	Elimination of cause, stretching, rest, ice , systemic or topical analgesics	rest, immobilization, systemic or topical analgesics	RICE, stretching, protective wraps, systemic or topical analgesics	RICE, stretching, protective wraps, systemic or topical analgesics	Light to moderate exercise, weight loss, systemic or topical analgesics

Carpal tunnel syndrome

Carpal tunnel syndrome is a common condition that causes pain, numbness, and tingling in the hand. The condition occurs when one of the major nerves to the hand — the median nerve — is squeezed or compressed as it travels through the wrist.



Carpal tunnel syndrome

- Heredity
- Repetitive hand use
- Hand and wrist position
- Pregnancy
- Health conditions



Carpal tunnel syndrome

- ▶ History of symptoms
- ▶ Physical examination
- ▶ Imaging
- ▶ Electromyography
- ▶ Nerve conduction study



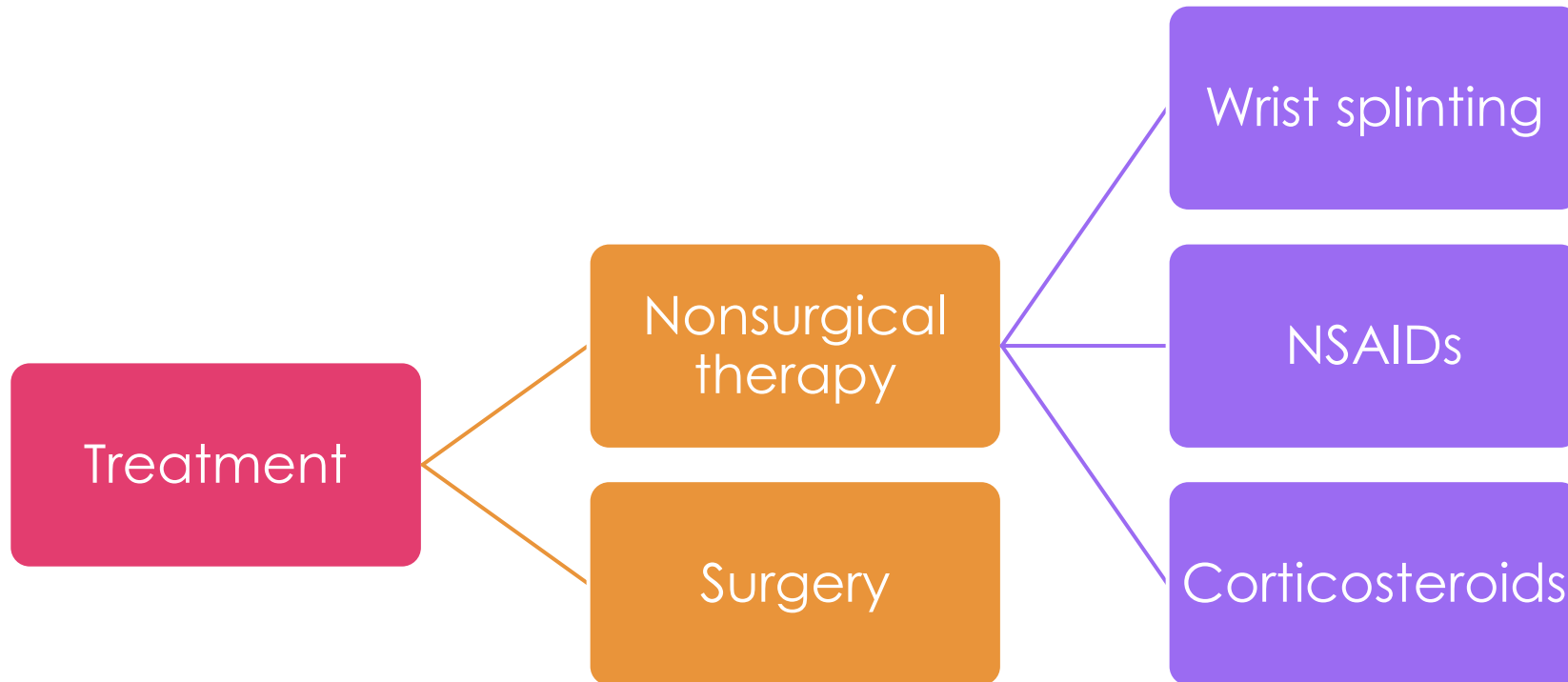
Grading the severity of CTS

Mild CTS

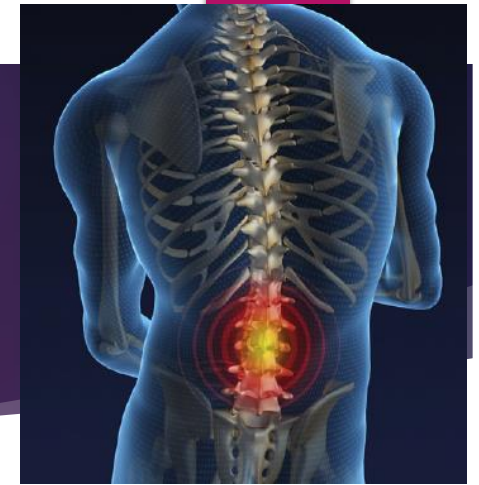
Moderate CTS

Severe CTS

Carpal tunnel syndrome

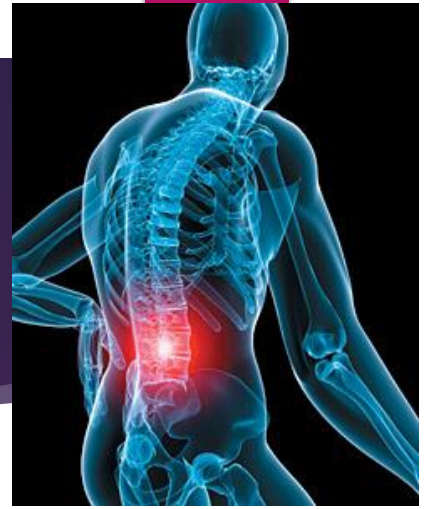


Low back pain



- ▶ Low back pain is extremely common. For example, in the US it is the fifth common reason patients see a medical practitioner and in the UK 7–8% of all adult GP consultations are for low back pain.
- ▶ Acute low back pain is self-limiting:
 - ❑ Over 90% of patients will get better within 6 weeks,
 - ❑ up to two-thirds of patients will have a recurrence within one year after initial onset
 - ❑ fewer than 5% of patients go on to develop back pain classed as chronic (persists for more than 12 weeks).

Prevalence and epidemiology

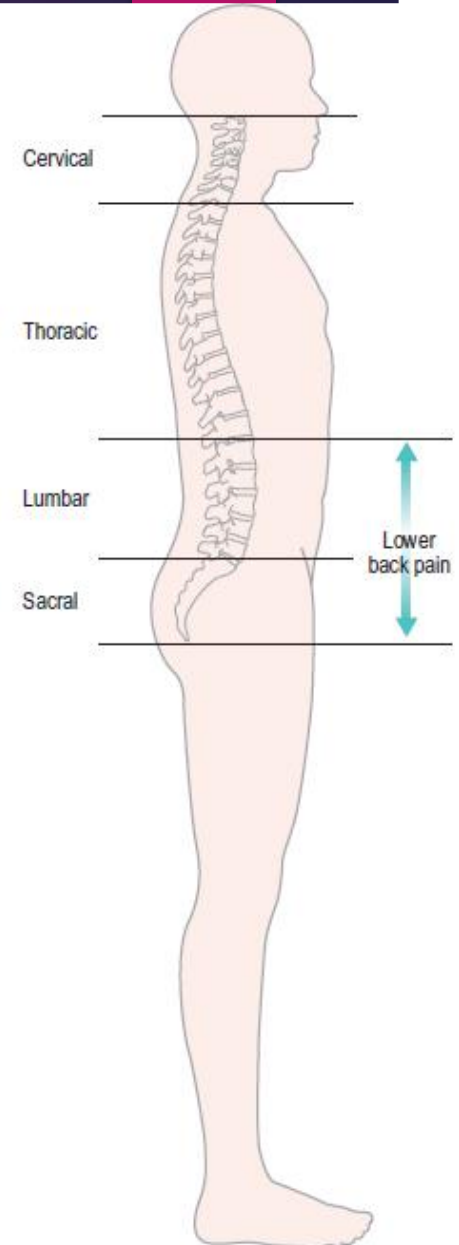


- ▶ common between the ages of 30 - 55 years with prevalence rates similar for men and women.
- ▶ 50% - 90% of pregnant women develop low back pain
- ▶ in developed countries 60% - 90% of adults will experience an episode of low back pain at some point in their adult lives.
- ▶ Occupational risk factors:
 - ▶ Heavy manual labour,
 - ▶ frequent bending, twisting and lifting
 - ▶ static positions for long periods of time
 - ▶ Sports, which involve excessive twisting, such as, golf and gymnastics can also lead to back pain.

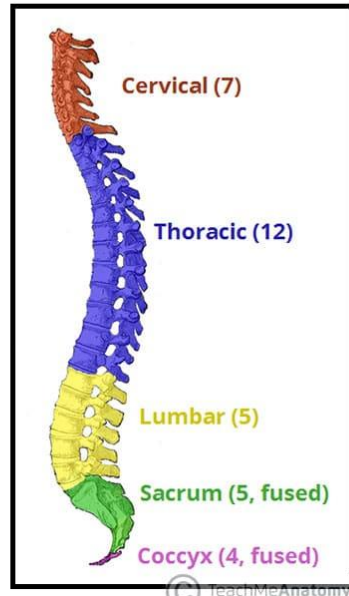
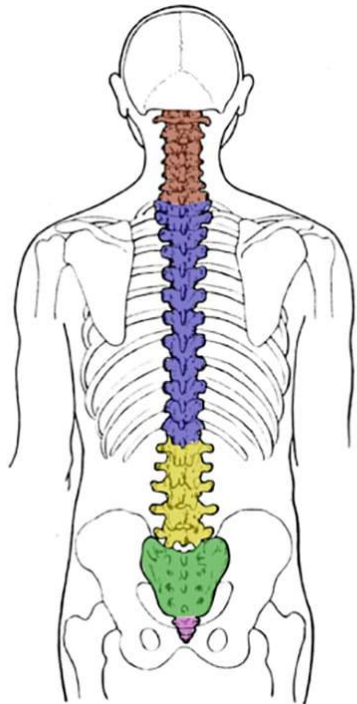
Etiology

- ▶ majority of patients (95%) who present in the pharmacy will have **simple back pain**.

Causes of back pain and their relative incidence in community pharmacy	
Incidence	Cause
Most likely	Simple back pain (usually associated with physical activity)
Likely	Nerve root compression (e.g. sciatica), pregnancy, (osteoarthritis)
Unlikely	Osteomyelitis, ankylosing spondylitis
Very unlikely	Malignancy



Etiology



Testing for lumbar nerve root compromise

Nerve root

L4

L5

S1

Pain



Numbness



Motor weakness

Extension of quadriceps

Dorsiflexion of great toe and foot

Plantar flexion of great toe and foot

Screening examination

Squat and rise

Heel walking

Walking on toes

Reflexes

Knee jerk diminished

None reliable

Ankle jerk diminished

TRIGGER POINTS indicative of referral

Symptoms/signs	Possible danger
Fever	Infection
Pain that radiates away from lower back area	Sciatica, discopathy
Young or older people (<20, and >55 years old) Numbness Persistent and progressively worsening pain Weight loss Feeling unwell	Possible sinister spinal pathology
Bowel or bladder incontinence	Cauda equina syndrome (rare and very unlikely)
Back pain from structures above the lumbar region	Outside scope of community pharmacist
Failure of symptoms to improve after 4 weeks	Requires further investigation as pain becoming sub acute (approx. 6 weeks duration) and requires medical intervention

Specific questions to ask the patient:

- ▶ Age

- ▶ Location:

- ❑ Pain that radiates into the buttocks, thighs and legs implies nerve root compression. If pain is felt below the knee, this is highly suggestive of sciatica.

- ▶ Onset:

- ❑ Low back pain that is acute and sudden in onset is likely to be muscle strain in the lumbosacral region and not serious.
- ❑ acute low back pain in the elderly should be referred as even slight trauma can result in compression fractures

Specific questions to ask the patient:

▶ Restriction of movement:

- ❑ People with **disc herniation** usually have difficulty in sitting down for long periods
- ❑ **Mechanical causes** of pain is exacerbated with physical activity and relieved by rest

▶ Weakness or numbness:

- ❑ **Progressive muscle weakness** must be referred for further evaluation

Non pharmacologic Therapies

- ▶ Heat
- ▶ Massage
- ▶ Acupuncture
- ▶ Spinal manipulation
- ▶ Exercise and physical therapy



Non pharmacologic Therapies???

- ▶ Cold
- ▶ Muscle energy technique
- ▶ Traction
- ▶ Lumbar supports
- ▶ Mattress recommendations
- ▶ Yoga
- ▶ Paraspinal injections

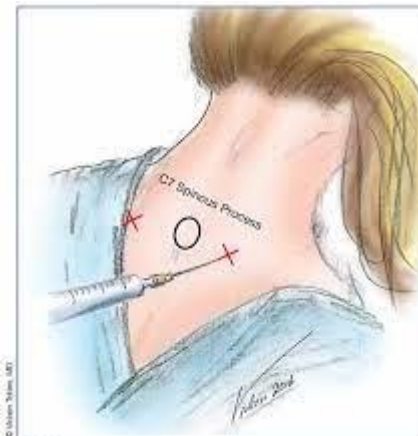


Figure 1



pharmacologic Therapies

➤ Initial therapy

❑ Nonsteroidal anti inflammatory drugs

- ibuprofen (400 to 600 mg four times daily) or
- naproxen (250 to 500 mg twice daily)

❑ Limited benefit of acetaminophen

- acetaminophen 650 mg orally every six hours as needed (maximum 3 grams per 24 hours)



pharmacologic Therapies

➤ Second-line therapy

❑ Combination with muscle relaxants

(benzodiazepines, cyclobenzaprine, methocarbamol, carisoprodol, baclofen, chlorzoxazone, metaxalone, orphenadrine, and tizanidine.)



pharmacologic Therapies



Efficacy

**Adverse
effects**

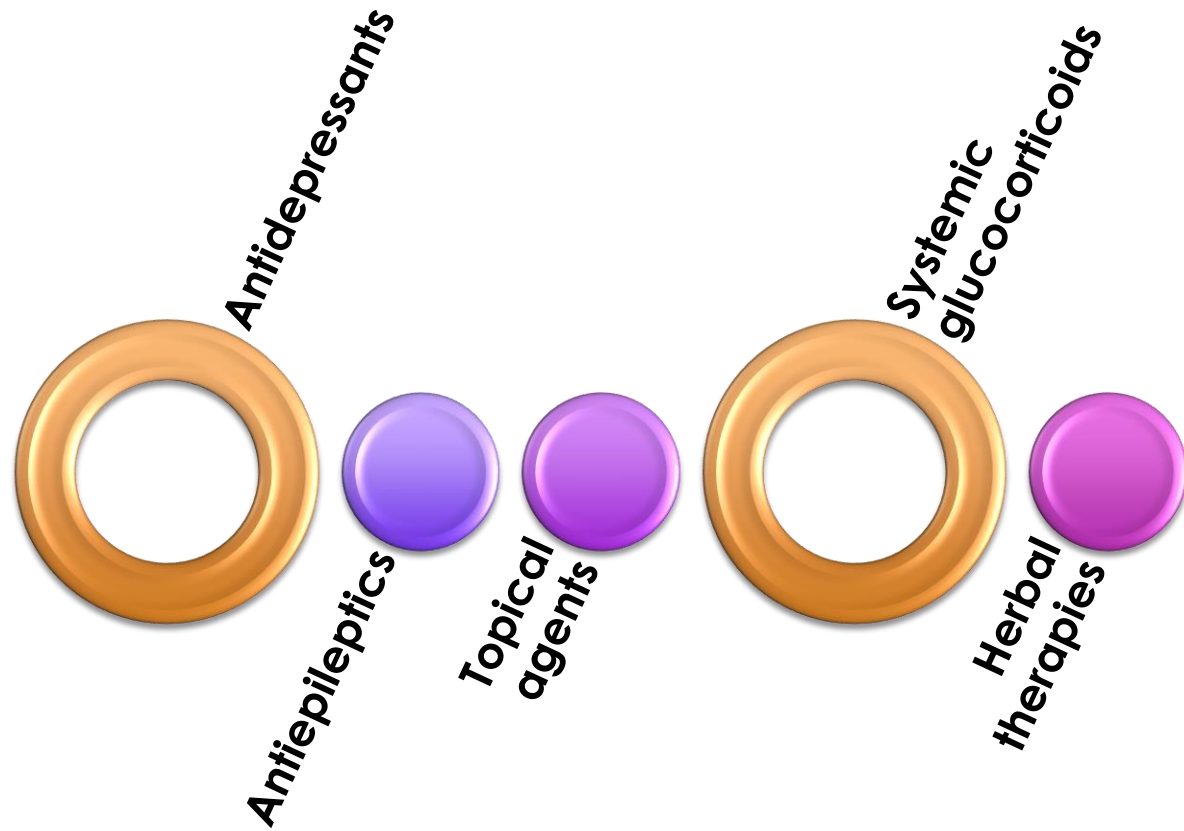
pharmacologic Therapies

Opioids

Tramadol

**Refractory or severe
pain**

pharmacologic Therapies



Pain management

Revised definition of pain

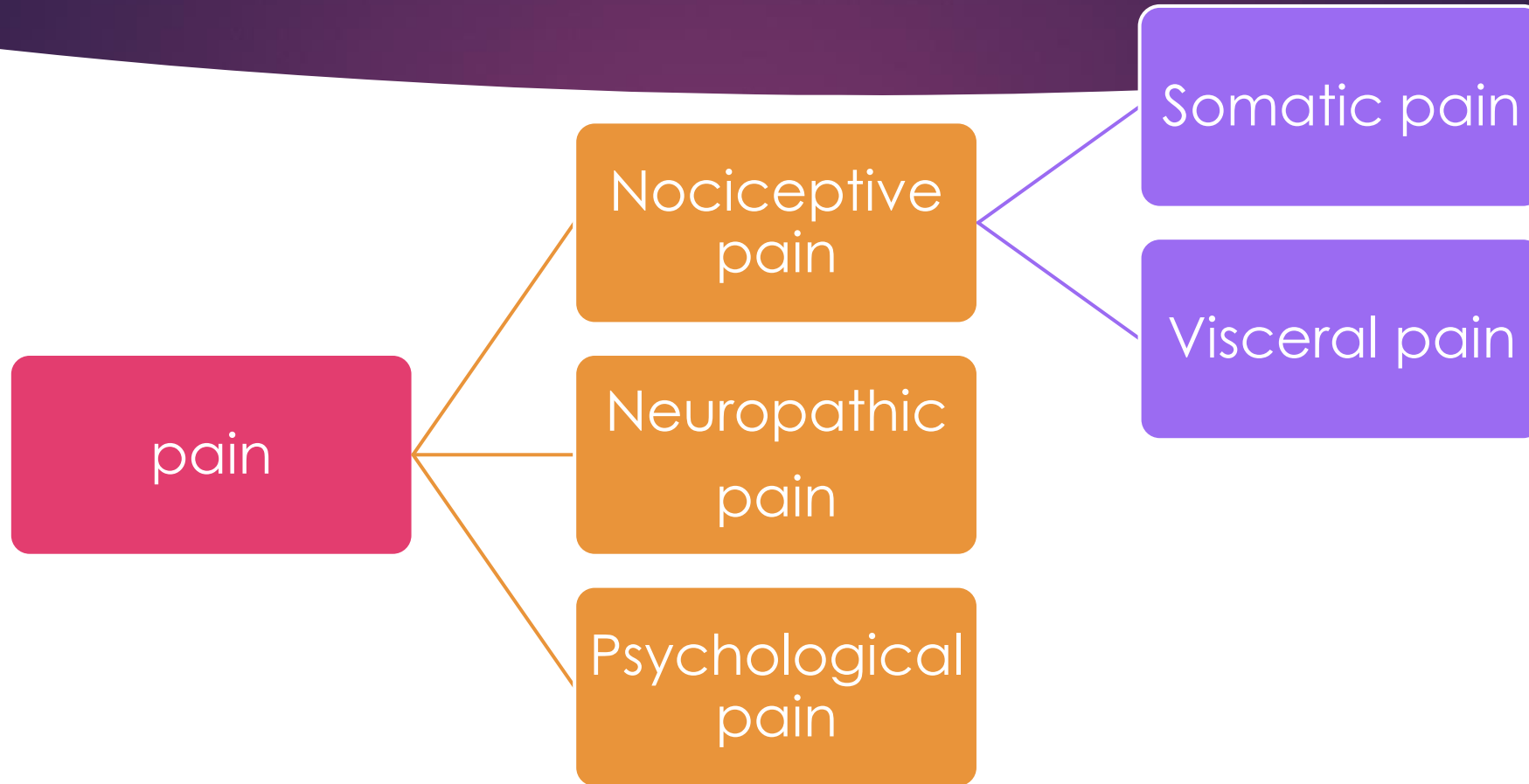
Pain

An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.

Notes

- Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
- Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
- Through their life experiences, individuals learn the concept of pain.
- A person's report of an experience as pain should be respected.^[1]
- Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
- Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.

Pain management

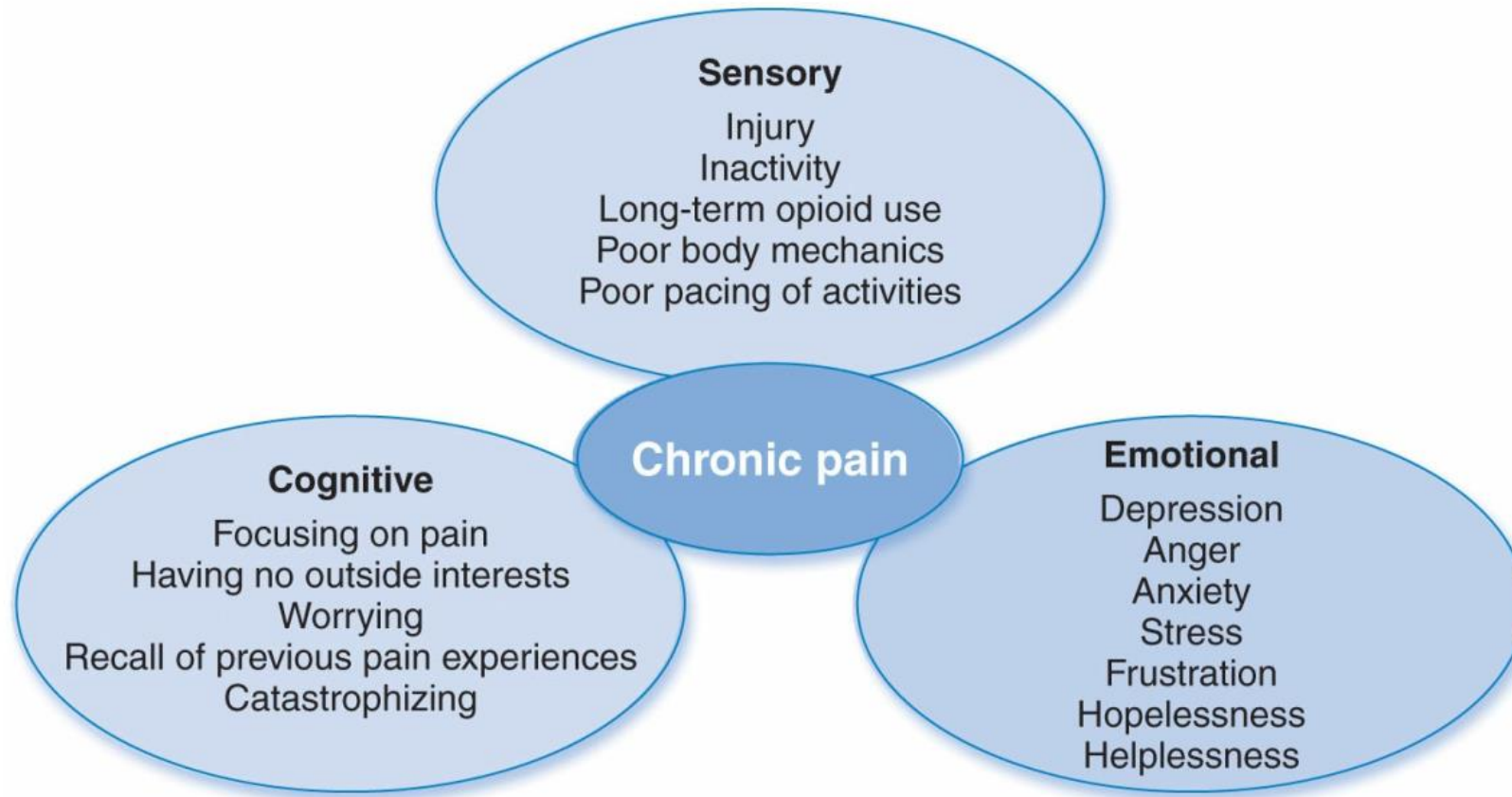


Pain management



Chronic pain affects more than **25%** of Americans over the age of **20 years**. Many people think that pain is a natural part of growing older, and up to 60% of people believe that pain is just something you have to live with.

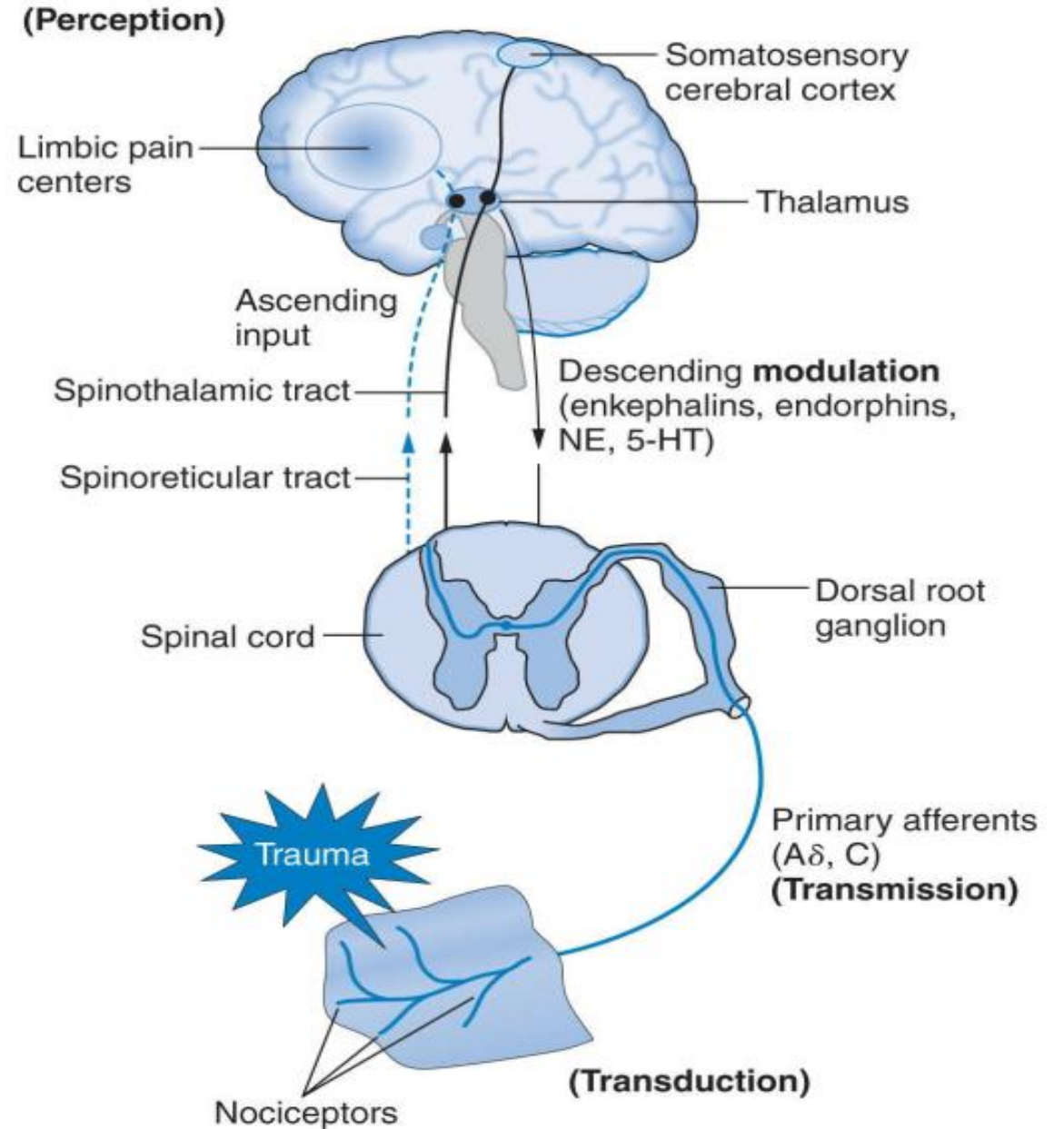
Pain management



Pain management

Nociception, or the sensation of pain, is composed of four basic processes:

- ▶ transduction,
- ▶ transmission,
- ▶ modulation,
- ▶ perception



Pain management

Mechanoreceptor and **chemoreceptors** mediate muscle pain.

Mediated by:

- ▶ **Histamine**
- ▶ Acetylcholine
- ▶ **Serotonin**
- ▶ **Bradykinin**
- ▶ adenosine
- ▶ potassium

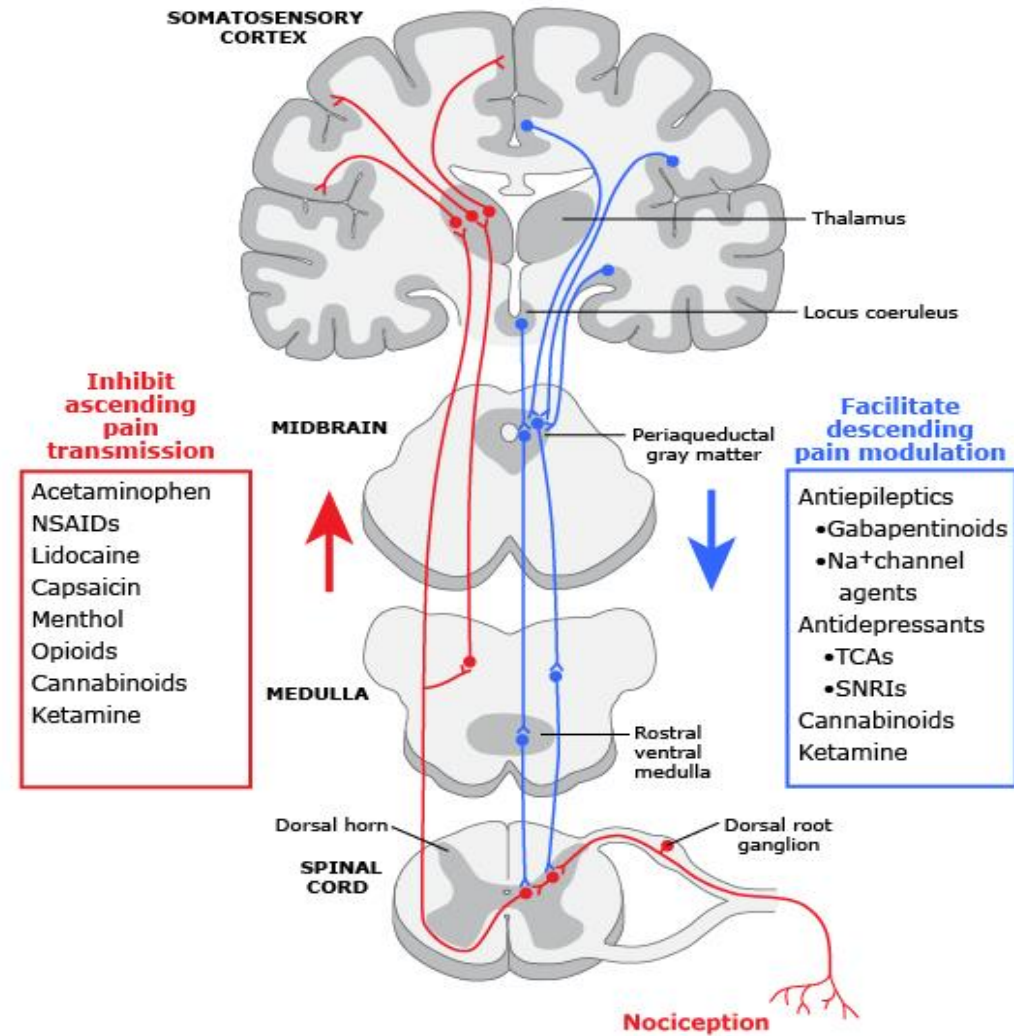


Redness (erythema) &
tenderness (hyperalgesia)

- Leukotriene
- Prostaglandin E

Pain management

Pain pathways [1-3]



NSAIDs: nonsteroidal antiinflammatory drugs; TCAs: tricyclic antidepressants; SNRIs: serotonin-norepinephrine reuptake inhibitors.

Pain management

Pain history

OLDCARTS

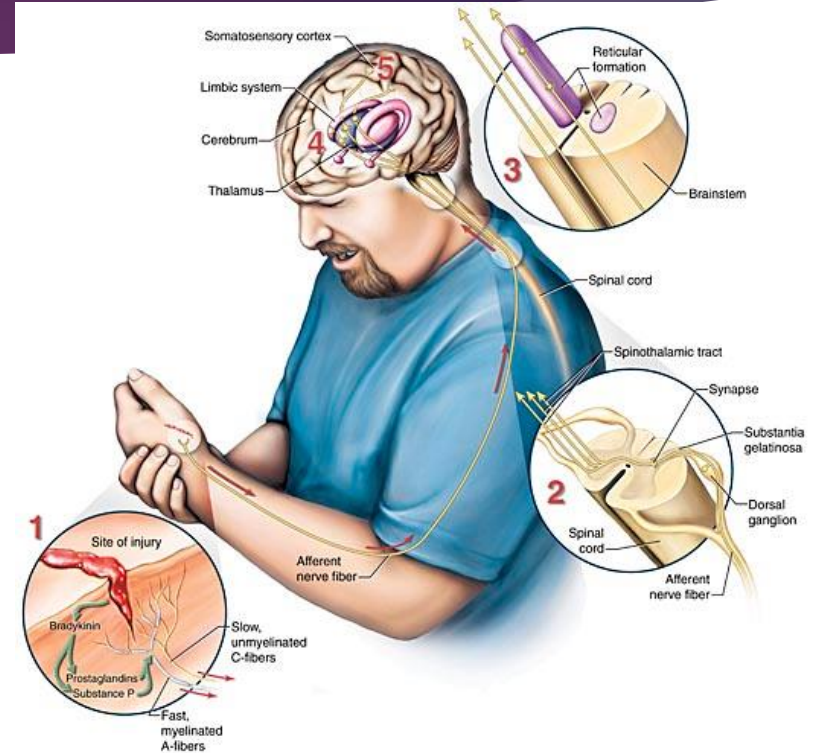
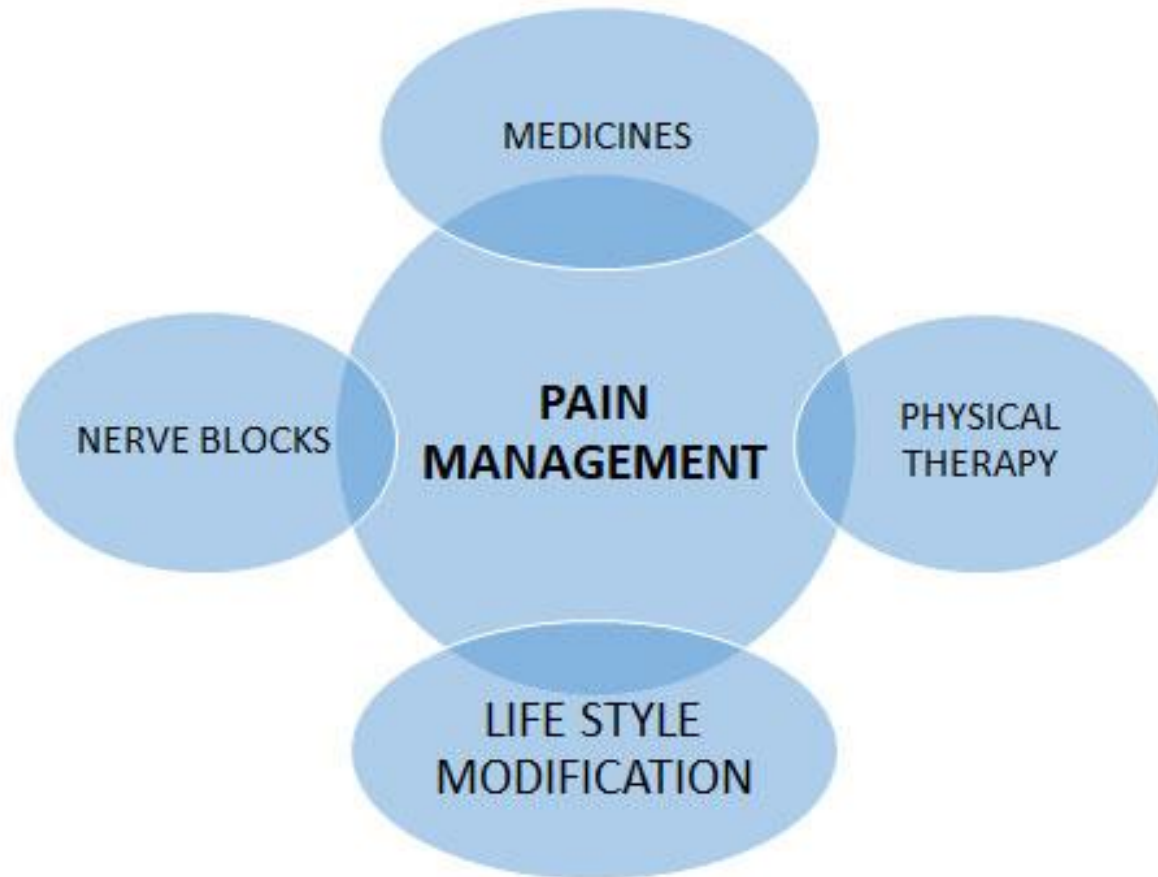
- Onset ("When did your pain start?")
- Location ("Where does it hurt?")
- Duration ("How long does your pain last?")
- Character ("How does your pain feel?", ie, aching, burning, shooting, tingling)
- Alleviating/Aggravating ("What makes your pain better/worse?") and Attribution ("What do you think is the cause?")
- Radiation ("Does this pain spread anywhere else?")
- Temporal pattern ("Does your pain vary over the course of a day?")
- Symptoms associated ("How does your pain impact your physical function, your mood, your sleep?")

Pain severity and impact

Pain intensity, pain interference with enjoyment of life and general function (PEG)

- What number (0 to 10) best describes your pain on average in the past week?
- What number (0 to 10) best describes how, in the past week, pain has interfered with your enjoyment of life?
- What number (0 to 10) best describes how, in the past week, pain has interfered with your general function?

Pain management



Pain management

Nonpharmacologic multimodal analgesia

- Cognitive behavioral: identify distressing negative cognitions and beliefs; increasing psychological flexibility, mindfulness-based stress reduction, relaxation training, biofeedback
- Physical: activity coaching, graded exercise (land and aquatic) with physical training, class, trainer, and/or solo; TENS use while physically active
- Spiritual: identify and seek meaningfulness and purpose of life
- Education (patient and family): improve health literacy, motivate patients to initiate and sustain efforts that increase function, mood, sleep, and quality of life.

TENS: transcutaneous electrical nerve stimulation.

Pharmacologic treatment based on type of pain [1,2]

Type of pain	First line therapy	Considerations for opioid use
Nociceptive	NSAIDs	When other treatment options are inadequate, for pain severe enough to require potentially daily, round the clock, long term treatment. Limit dose and duration whenever possible. Encourage as-needed use linked to meeting specific activity goals
Neuropathic	Antidepressants (TCAs or SNRIs) or Antiepileptic drugs	
Central sensitization	Antidepressants (TCAs or SNRIs) or Antiepileptic drugs	Avoid whenever other multidisciplinary treatment options have not been systematically, sufficiently and consistently trialed. Opioids often worsen central sensitization treatment outcomes.

NSAIDs: nonsteroidal antiinflammatory drugs; TCAs: tricyclic antidepressant; SNRIs: serotonin-norepinephrine reuptake inhibitors.

Acetaminophen

Drug	Optional initial loading dose*	Usual analgesic dose (oral)	Maximum dose per day (mg)	Selected characteristics and role in therapy
Para-aminophenol derivative				
Acetaminophen(paracetamol)	None	325 to 650 mg every 4 to 6 hours Or 1000 mg every 6 hours up to three times per day	3000 mg	<ul style="list-style-type: none"> ▪ Effective for noninflammatory pain; may be opioid-sparing. ▪ Doses <2000 mg per day do not increase risk of serious GI complications. ▪ Does not alter platelet functioning. ▪ Can cause hepatotoxicity in chronic or acute overdose. ▪ Avoid or use a lower total daily dose (maximum 2000 mg per day) in older adults, patients at risk for hepatotoxicity (eg, regular alcohol use, malnourished) or with organ dysfunction. ▪ For short-term or one-time use, may use a total dose of up to 4000 mg per day in selected medically supervised patients. ▪ Interacts with warfarin (prolongs INR), isoniazid, and CYP450-inducing drugs[¶] (transaminitis). ▪ Warn patients about acetaminophen content in combination prescription (eg, oxycodone-acetaminophen) and OTC preparations.

Acetaminophen

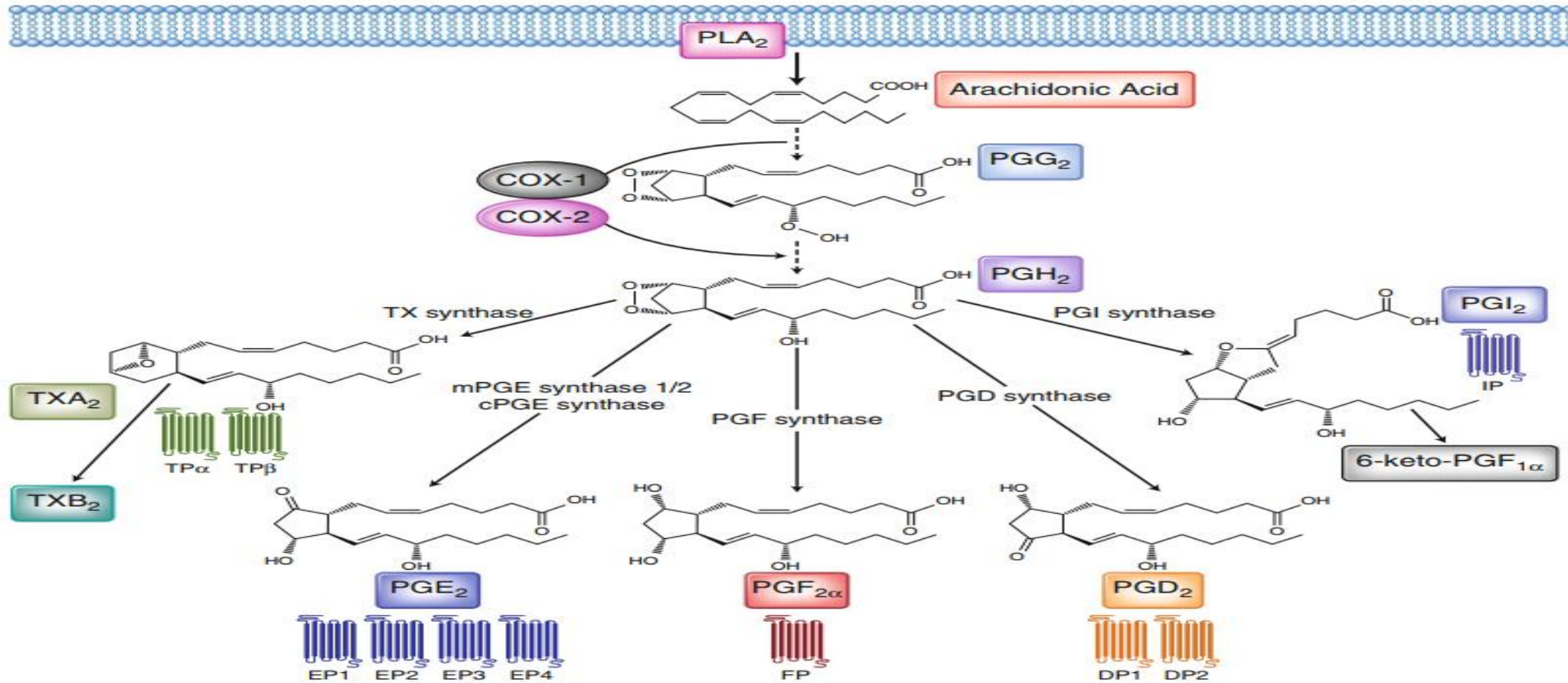
Although not fully elucidated, the analgesic effects are believed to be due to activation of descending serotonergic inhibitory pathways in the CNS. Interactions with other nociceptive systems may be involved as well. Antipyretic is produced from inhibition of the hypothalamic heat-regulating center.

Acetaminophen

- ▶ TABLET ORAL: 325 mg, 500 mg
- ▶ EFFERVESCENT ORAL: 500 mg
- ▶ DROPS SOLUTION ORAL: 100 mg/1mL(15ml)
- ▶ DROPS SUSPENSION ORAL: 100 mg/1mL(15ml)
- ▶ SOLUTION ORAL: 120 mg/5mL(60ml) (120ml)
- ▶ SUSPENSION ORAL: 120 mg/5mL (120ml)
- ▶ SUPPOSITORY RECTAL:125 mg, 325 mg
- ▶ SOLUTION INTRAVENOUS: 10 mg/1mL (100ml)
- ▶ CONCENTRATE SOLUTION INTRAVENOUS: 150 mg/1mL (6.7ml)

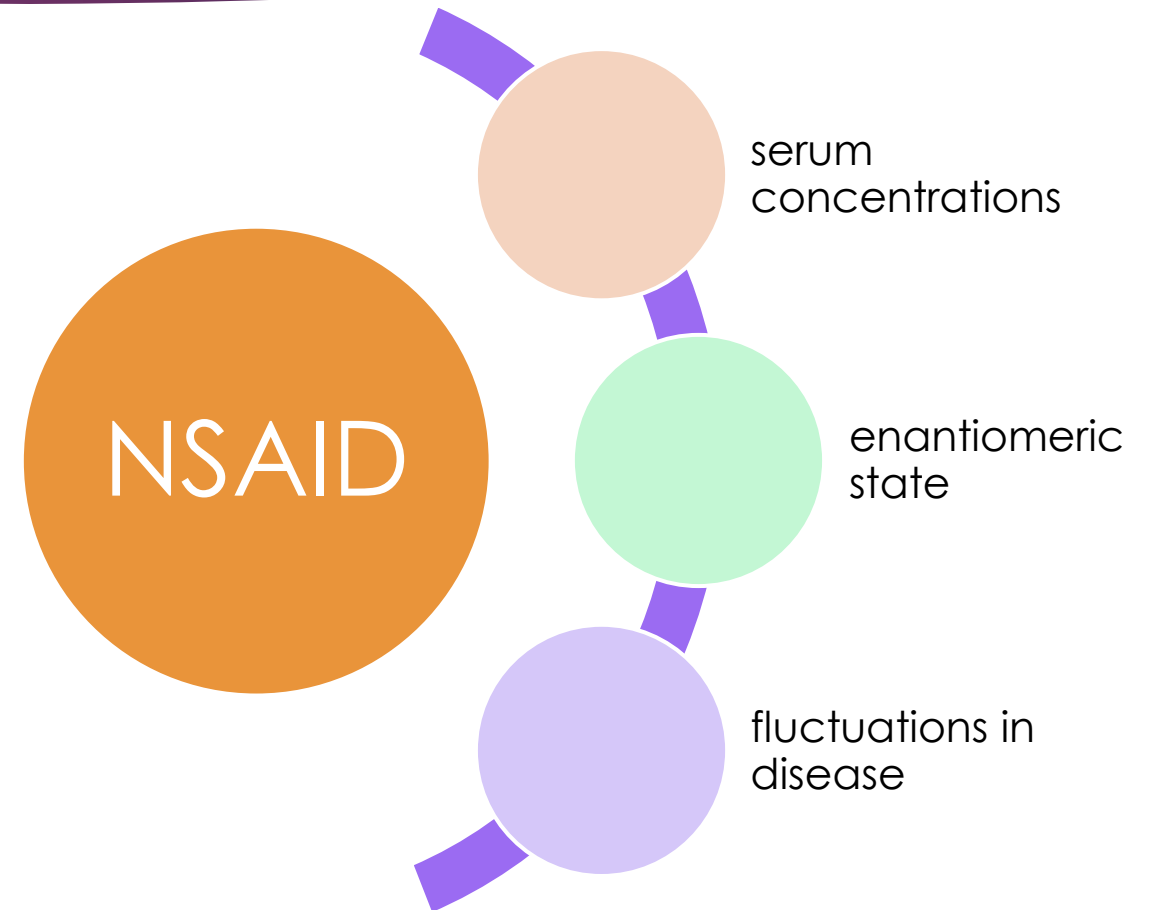


NSAIDs

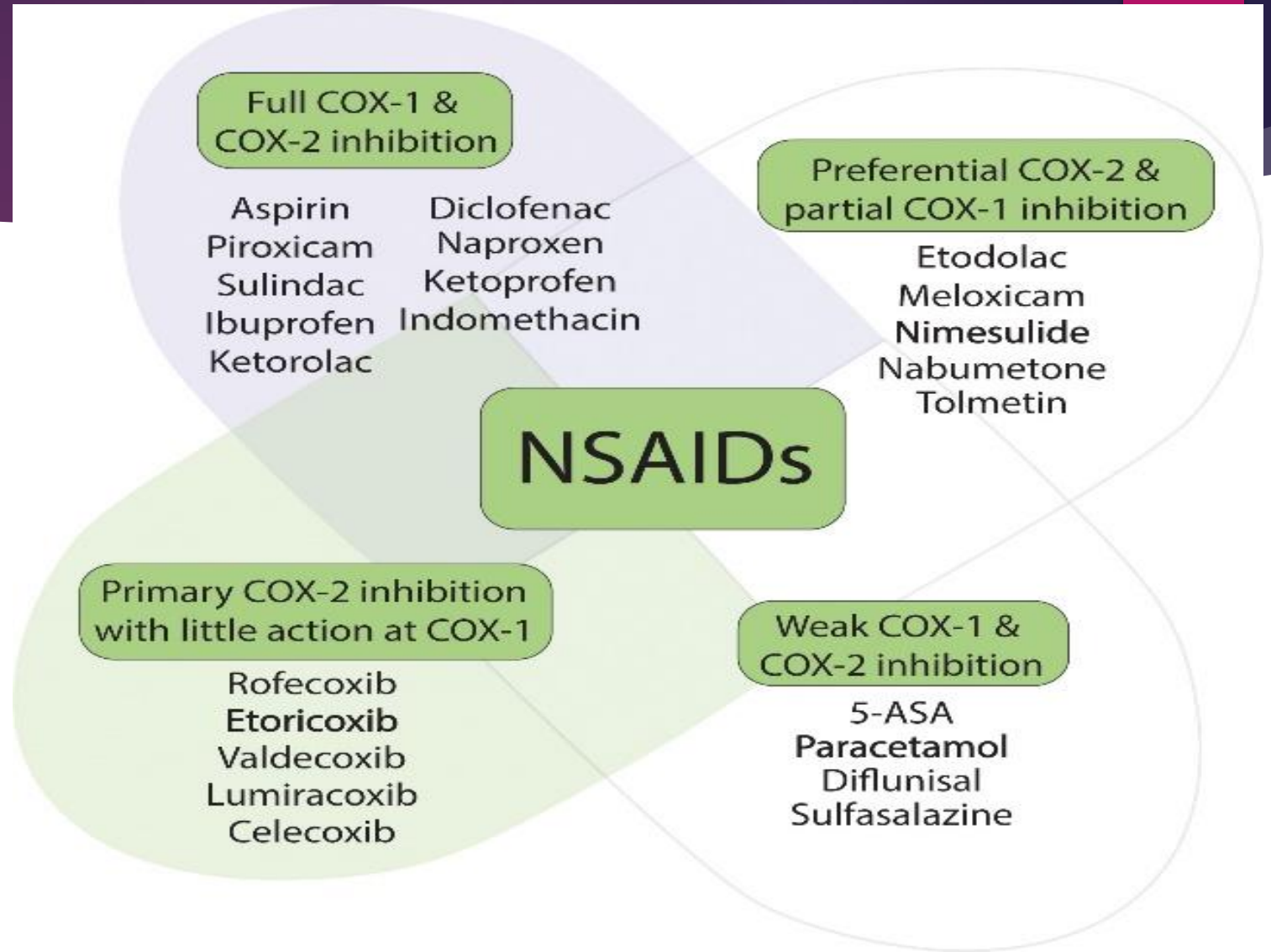


NSAIDs

The risk of adverse events seems to vary between individual drugs and patients; these differences in adverse event risk have been ascribed to differences in pharmacokinetics.



NSAIDs



NSAIDs

Salicylates

- Aspirin Diflunisal
- Na.salicylate salicylamide

Para-aminophenol

- Acetaminophen

Phenyl Acetic acid

- Diclofenac
- Ketorolac

Oxicams

- Piroxicam

Pyrazolone derivatives

- Phenylbutazone Oxyphenbutazone
- Analgin Azapropazone

Propionic acid derivatives

- Ibuprofen Ketoprofen Flurbiprofen
- Naproxen

Fenamates

- Mafenamic acid
- Flufenamic acid

Preferential COX-2 inhibitors

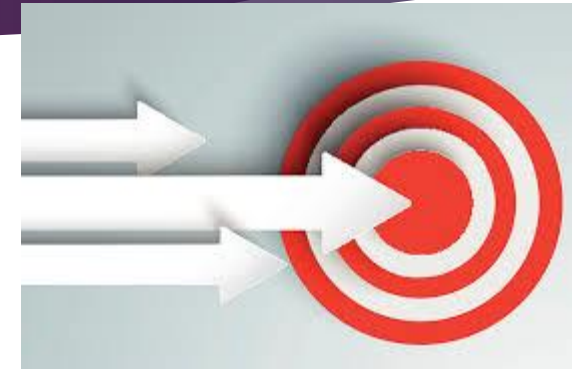
- Nimesulide
- Meloxicam Nebumatone

Selective COX-2 inhibitors

- Celecoxib Rofecoxib
- Paracoxib Lumiracoxib Valdecoxib

NSAIDs

- ▶ Effective for treatment of ...
- ▶ risk of gastropathy
- ▶ renal impairment
- ▶ reversibly inhibit platelet functioning
- ▶ Avoid NSAIDs in patients with ...
- ▶ caution



NSAIDs



ASA and
other
NSAIDs

NSAIDs

Generic Name	Usual analgesic dose(oral)	Maximum Daily Dose (mg)
Aspirin	325 to 650 mg every 4 to 6 hours	4,000
Ibuprofen(Motrin)	400 mg every 4 to 6 hours	3,200
Naproxen	250 to 500 mg every 12 hours	1,500
Mefenamic acid	250 mg every 6 hours	1000
Diclofenac(Voltaren)	50 mg every 8 hours	200
Indomethacin	IR: 25 to 50 mg every 8 to 12 hours CR: 75 mg once or twice daily	150
Sulindac (Clinoril)	150 to 200 mg every 12 hours	400
Tolmetin (Tolectin)	400 to 600 mg every 8 hours	1,800
Piroxicam (Feldene)	10 to 20 mg once daily	20
Meloxicam (Mobic)	7.5 to 15 mg once daily	15
Celecoxib (Celebrex)	200 mg daily or 100 mg every 12 hour	400

NSAIDs

In patients who experience an inadequate response to an NSAID of one class, the substitution of an NSAID of a different class is a reasonable therapeutic option. However, this strategy has never been evaluated in a prospective well-controlled study. Each attempt to achieve a response should last for about **two weeks**; this duration is based upon limited data and clinical experience.

Compound analgesics

(acetaminophen /codeine)

(acetaminophen /caffeine)

(acetaminophen /codeine/ caffeine)

(acetaminophen /caffeine/ibuprofen)

- ▶ It is recognized that combination analgesics with high doses of opioids are effective in acute and chronic pain.
- ▶ doses are too low to produce statistically significant reductions in pain compared to single agents. However, the opioid dose might be sufficient to cause side effects such as constipation.
- ▶ Elderly patients are particularly susceptible to opioid side effects



Pain management

Mechanisms of action of drugs used for neuropathic pain

- | |
|---|
| ■ Gabapentin/pregabalin: Modulate voltage-gated calcium channels |
| ■ Carbamazepine/oxcarbazepine: Block voltage-dependent sodium channels |
| ■ Tricyclic antidepressants: Inhibit NE>5-HT reuptake, block sodium and calcium channels and NMDA receptors |
| ■ 5-HT/NE reuptake inhibitors: Inhibit 5-HT/NE reuptake |

NE: norepinephrine; 5-HT: 5 hydroxytryptamine (serotonin).

Recommended drug classes for treatment of neuropathic pain

Drug	Effective dose	Comments
First-line therapy		
Antiepileptic drugs		<ul style="list-style-type: none"> Can cause dizziness and sedation; minimize with slow titration Use lower doses for older patients Avoid concomitant use with opioids; can cause respiratory depression
Gabapentin	<ul style="list-style-type: none"> IR: 300 to 1200 mg orally three times daily ER: 600 to 1800 mg orally twice daily 	<ul style="list-style-type: none"> Initiate treatment at a low dose (typically 300 mg orally at night), increasing gradually until pain relief or limiting side effects occur
Pregabalin	<ul style="list-style-type: none"> 150 to 300 mg orally twice daily 	<ul style="list-style-type: none"> Initiate treatment at low dose (typically 150 mg orally at night)
Antidepressants		
Serotonin-noradrenaline reuptake inhibitors		
Duloxetine	<ul style="list-style-type: none"> IR: 60 to 120 mg orally once daily 	
Venlafaxine	<ul style="list-style-type: none"> ER: 75 to 225 mg orally once daily 	
Tricyclic antidepressants (TCAs)		
Nortriptyline	<ul style="list-style-type: none"> 25 to 75 mg orally once daily 	<ul style="list-style-type: none"> Initiate treatment at low dose, increase slowly at weekly intervals May take 6 to 8 weeks, including 2 weeks at highest tolerated dose, for adequate trial
Amitriptyline	<ul style="list-style-type: none"> 25 to 125 mg orally once daily 	<ul style="list-style-type: none"> Preferred among TCAs due to less sedation and fewer anticholinergic effects Most sedating TCA
Second-line therapy		
Capsaicin 8% patch	<ul style="list-style-type: none"> 1 to 4 patches to painful area for 30 to 60 minutes every three months 	<ul style="list-style-type: none"> For peripheral pain Long term safety not established
Lidocaine patch	<ul style="list-style-type: none"> 1 to 3 patches to painful area for ≤ 12 hours in a 24 hour period, patch-free period of ≥ 12 hours 	<ul style="list-style-type: none"> For peripheral pain
Tramadol	<ul style="list-style-type: none"> IR: 100 to 200 mg orally three times daily ER: 100 to 200 mg orally twice daily 	
Third-line therapy		
Botulinum toxin A	<ul style="list-style-type: none"> 50 to 200 units subcutaneously to painful area every 3 months 	<ul style="list-style-type: none"> Specialist use, for peripheral pain
Strong opioids	<ul style="list-style-type: none"> Individual titration 	<ul style="list-style-type: none"> Not routinely used for chronic pain Use only at lowest effective dose, after risk assessment, and with ongoing assessment of risks and benefits Use in combination with nonpharmacologic and nonopioid pharmacologic therapy

IR: immediate release; ER: extended release.

Pain management

TCAs or SNRIs are indicated for treatment of pain even in the absence of mood disturbance. **Analgesic antidepressants** provide pain relief separate from their antidepressant effects, with analgesic effects known to occur in non-depressed patients. However, for some patients, an effect on underlying depression, especially for SSRIs, may also contribute to relief of pain

Pain management

The choice among treatments should be individualized based on the **pain condition** (if known), **patient-specific characteristics**, **comorbid conditions**, **medication side effect profile**, **cost**, and **patient values and preferences**. In practice, comorbidities and concurrent medications often favor one drug class or another (eg, start with an antidepressant if the patient is also depressed or anxious, or a gabapentinoid when antidepressant drug-interactions or side-effects are problematic).

Pain management



Combination therapy with both antidepressant and antiepileptic drugs is **often required**, because less than **one-half** of patients with neuropathic pain will respond to a single agent. However, evidence is scant regarding the efficacy of specific combinations and the safety of combination treatment

Pain management

Tapering and discontinuing antidepressants can be challenging. Abruptly stopping or rapidly tapering can cause a variety of symptoms, including agitation, anxiety, chills, diaphoresis, dizziness, dysphoria, fatigue, headache, insomnia, irritability, myalgias, nausea, paresthesias, rhinorrhea, and tremor.

A very slow tapering schedule over 2 to 4 weeks is recommended

Pain management

- ▶ 3 antiepileptic drugs (gabapentin, pregabalin, and carbamazepine) are drugs approved by the (FDA)
- ▶ gradual increases until pain relief or dose-limiting adverse effects
- ▶ Pregabalin may provide analgesia more quickly than gabapentin
 - ▶ lower initial dose may be efficacious
 - ▶ a shorter time is required to titrate to a full dose
- ▶ An adequate trial of treatment
- ▶ Adjustment



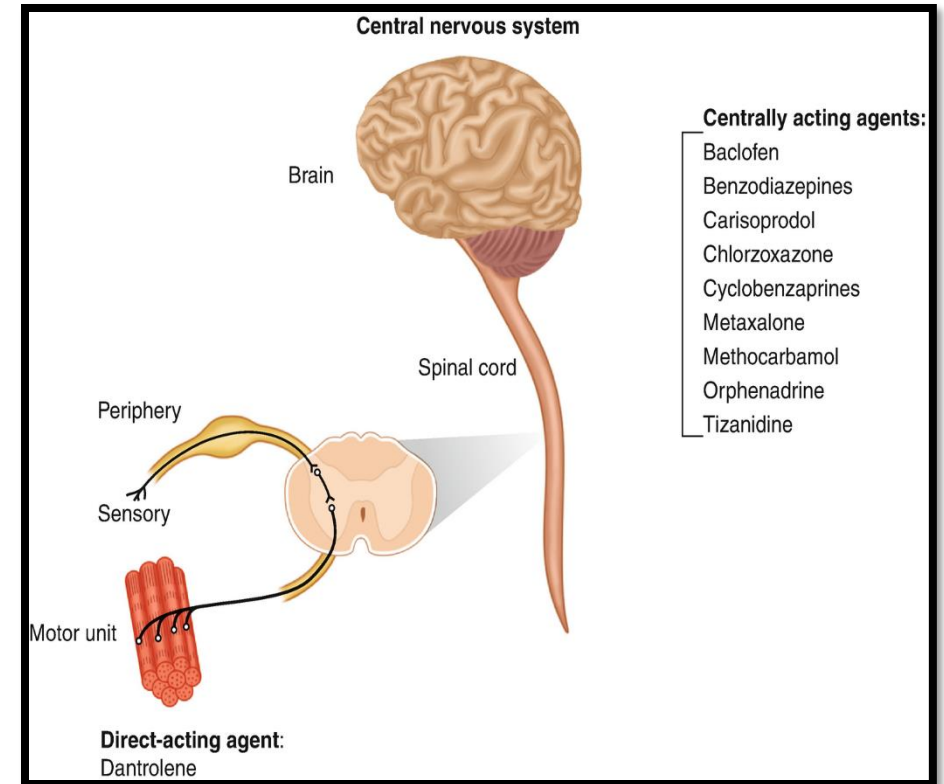
Pain management

Opioids should be considered a **second- or third-line** option, especially when there is an expectation that they may be prescribed long-term. Opioids may be considered earlier in the treatment of select patients, such as those with **high severity intractable pain, episodic exacerbations of severe pain, or neuropathic cancer pain.**



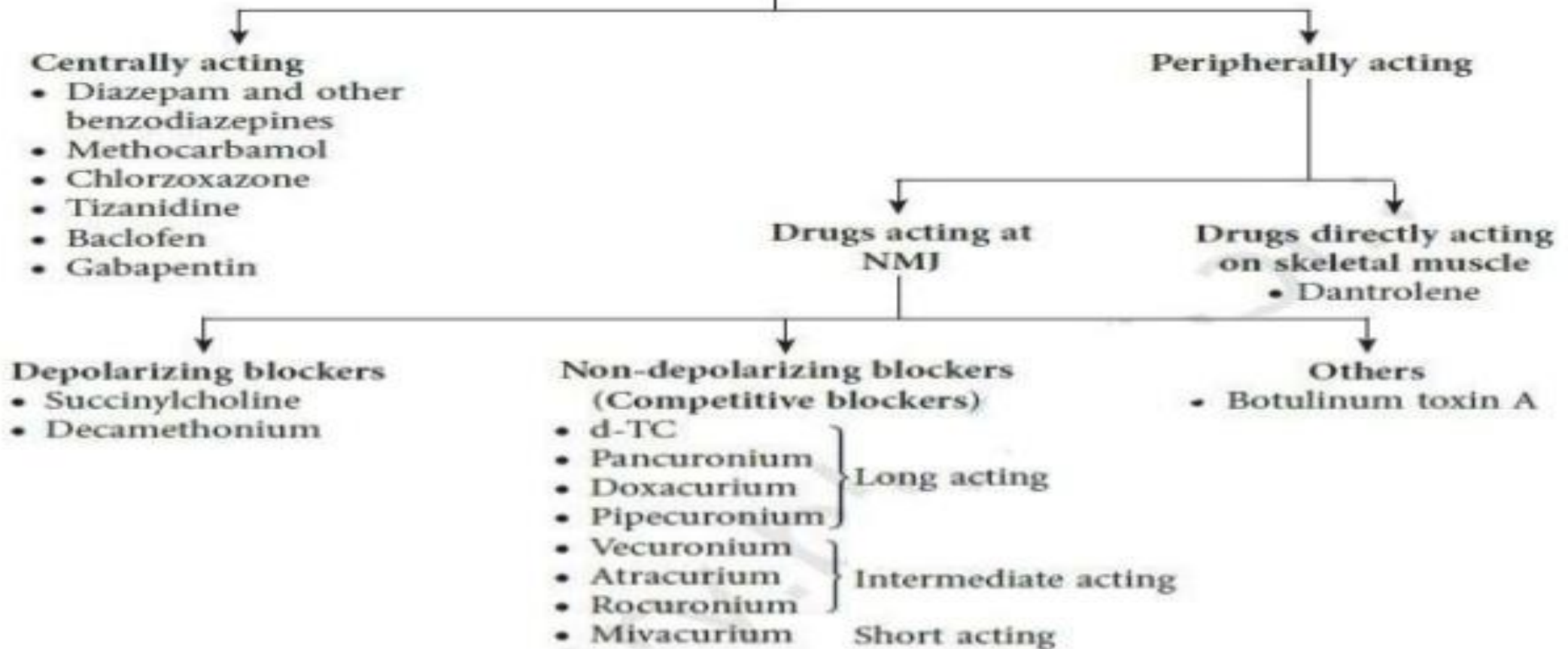
Oral Muscle Relaxants

- ▶ **Muscle Relaxants** are commonly used to treat chronic musculoskeletal pain. But Guidelines **do not recommend** chronic use of muscle relaxants for musculoskeletal pain.



Classification

Skeletal muscle relaxants



Muscle Relaxants

We avoid the use of benzodiazepines in patients with chronic pain, including those with anxiety or post-traumatic stress disorder. Benzodiazepines are not first-line anxiolytics or sleep aids and there is no evidence of analgesic efficacy for chronic pain.



Drug	Dose	Adverse Effects	Monitoring/Comments
Methocarbamol	1,500 mg TID, or 1,000 mg QID	rash, indigestion, N/V, dizziness, headache, somnolence, vertigo, blurred vision, arrhythmias, hypotension, leucopenia	Monitor heart rate, blood pressure
Tizanidine	4 mg TID	Hypotension, somnolence, muscle weakness	Monitor blood pressure, liver function
Baclofen	10 mg TID, titrate to max of 20 mg QID	Somnolence, muscle weakness, ataxia	
Dantrolene	25 mg daily × 7 days, 25 mg TID × 7 days, titrate to max of 100 mg QID	Hepatitis, tachycardia, confusion, nausea, vomiting, depression, fatigue, dizziness, somnolence, blood dyscrasias, rash, GI obstruction	Monitor liver function



Thank you for your enthusiasm!

neuromuscular blocking medications

Indications for the use of neuromuscular blocking agents

To **facilitate short procedures** under general anesthesia (endotracheal intubation, bronchoscopy, gastrointestinal endoscopy, specialized radiologic procedures)

To **facilitate mechanical ventilation** (increase chest wall compliance, prevent poorly coordinated respiratory movements, reduce peak airway pressures, and facilitate permissive hypercapnia) despite adequate sedation and analgesia

To reduce **muscle oxygen consumption**

To **prevent respiratory or other movements**, and coughing on tracheal suction in patients with increased intracranial pressure or massive hemoptysis

To facilitate treatment of medical conditions associated with increased muscle activity, including **tetanus, neuroleptic malignant syndrome, or status epilepticus**

neuromuscular blocking medications

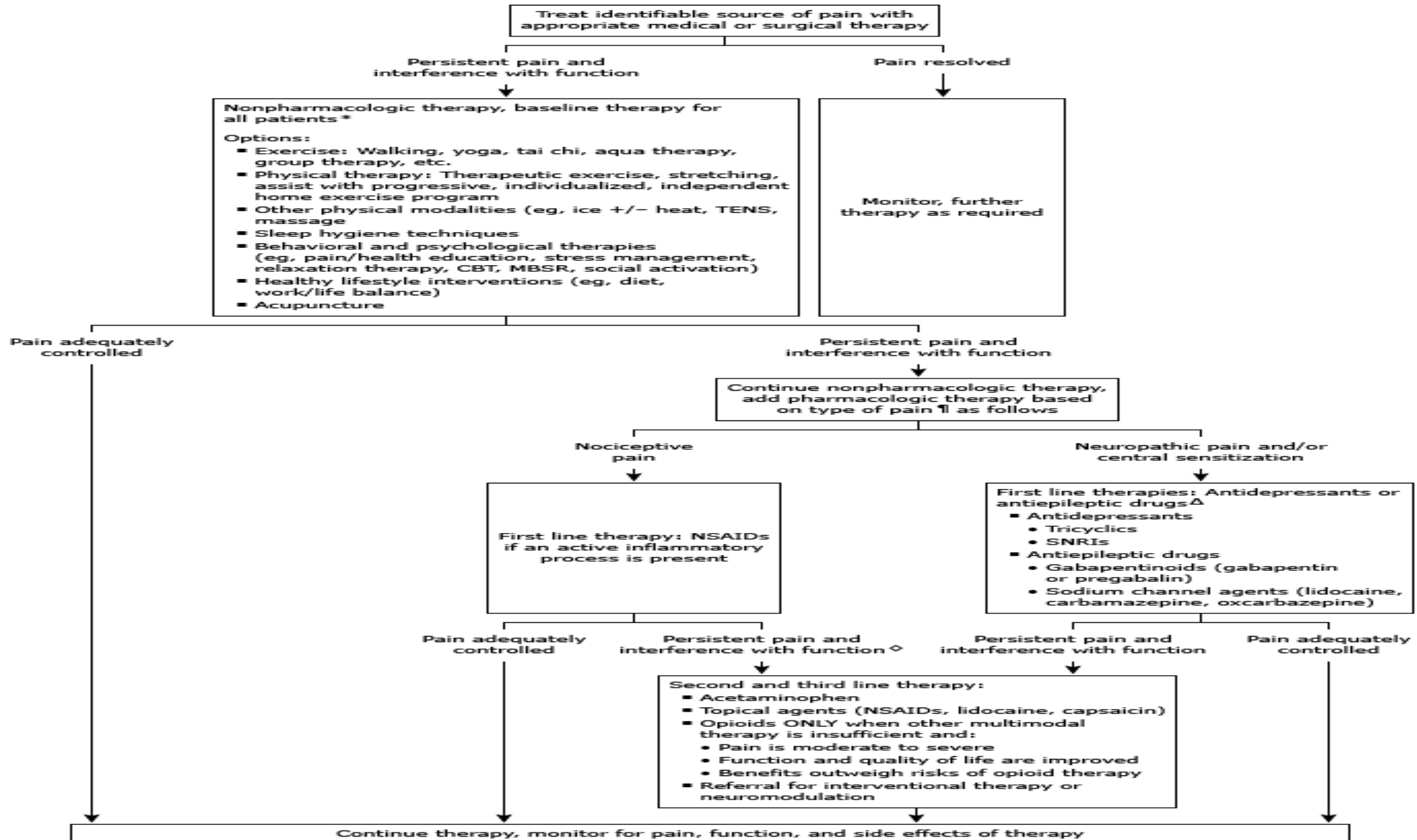
Drug	Duration of action	Onset (min)	Elimination (% renal)	Elimination (other)	Half-life(min)			
					Normal	Renal Failure	Hepatic Failure	Elderly
Atracurium	intermediate	2.0-2.5	<10	Ho, EH	21	↔	↔	↔
Cisatracurium	intermediate	3.0-6.0	<20	Ho	22-29			↑
Mivacurium	short	1.5-2.5	<10	EH	2-5	↑	↑*	↑
Pancuronium	long	1.0-3.0	60-80	H	100-130	↑	↑	↑
Pipecuronium	long	1.5-3.0	60-90		120-150	↑		
Rocuronium	intermediate	1.0-1.5	<10	H	60-100	↔	↑	↑
Vecuronium	intermediate	1.5-3.0	10-20	H	80-90	↔	↔	↑

neuromuscular blocking medications

Selecting an agent:

- ▶ Normal hepatic and renal function – Pancuronium is the drug of choice for patients with normal hepatic and renal function who require paralysis for more than one hour
- ▶ Hepatic and/or renal insufficiency – Atracurium or Cisatracurium is preferred in patients with hepatic and/or renal insufficiency.
- ▶ Cardiovascular disease – Vecuronium has the least adverse cardiovascular effects and is the drug of choice for patients with cardiovascular disease or hemodynamic instability. Pipecuronium and Rocuronium are acceptable alternatives

Algorithm: Chronic non-cancer pain diagnosis-targeted therapy



IBUPROFEN

- ▶ TABLET ORAL : 200,400 mg
- ▶ TABLET, EXTENDED RELEASE ORAL: 800 mg
- ▶ SUSPENSION ORAL: 100 mg/5mL (120ml)
- ▶ GEL TOPICAL: 5 % 60g
- ▶ INJECTION PARENTERAL: 100 mg/1mL (4,8ml)

