ZSMU

Department of general practice – family medicine

The medical help in the case of pain syndrome

Pain

- is a universally understood sign of disease;
- it is also the most common symptom that causes people to seek medical attention.
- "an unpleasant sensory and emotional experience [that is] associated with actual or potential tissue damage, or described in terms of such damage “ [The International Association for the Study of Pain (IASP)]
- It is possible to describe different types of pain, and each pain type tends to have a different presentation.
- The history and physical examination help clinicians to identify these differences.
- Precise and systematic pain assessment is required to make the correct diagnosis and thus to establish the most efficacious treatment plan for patients who present with pain.

- The somatosensory system involves the conscious perception of touch, pressure, pain, temperature, position, movement, and vibration that arises from the muscles, joints, skin, and fascia.
- This 3-neuron, 2-relay sites system carries sensations detected in the periphery through spinal cord-, brainstem-, and thalamic-relay nuclei pathways to the sensory cortex in the parietal lobe.
- Impulses from receptors travel via sensory afferents to the dorsal root ganglia, the site of the first-order neuron cell bodies.
- Their axons then travel ipsilaterally or contralaterally via the spinal cord.

- Second-order neuron cell bodies are located in the dorsal horn and medullary nuclei.
- Third-order neurons are located in the thalamus.
- The functional magnetic resonance image (fMRI) shows blood oxygen level-dependent (BOLD) responses to pulsed peripheral ultrasonographic stimulation (PUNS-M) of somatosensory circuits in 5 patients (aMCC, anterior middle cingulate cortex; Cdt, caudate; In, insula; Op, parietal operculum; Put, putamen; S1, primary somatosensory cortex; SMA, supplementary motor area; SMg, supramarginal gyrus; Th, thalamus).

Image courtesy of Legon et al.[6]

Pain Etiology

The categories of pain

- nociceptive
- neuropathic
- psychogenic

Different types of pain tend to respond to different treatments, the identification of pain type during pain assessment is important.

Nociceptive pain

- Nociception is a normal physiologic response to stimuli initiated by nociceptors, which detect mechanical, thermal, or chemical changes
- Nociceptive pain arises from activation of nociceptors.
- Nociceptors are found in all tissues except the central nervous system (CNS).
- The pain is clinically proportional to the degree of activation of afferent pain fibers and can be acute or chronic (eg, somatic pain, cancer pain, postoperative pain).
- It is caused by nerve injury or disease, as well as by involvement of nerves in other disease processes (eg, tumor, inflammation).
- Neuropathic pain may occur in the periphery or the CNS.

- **Nociceptive pain** :
- superficial somatic pain from cutaneous nociceptors on the skin or superficial tissues; it is typically localized and is described as throbbing, aching, or sharp/gnawing
- deep somatic pain from somatic nociceptors on ligaments, bones, blood vessels, and muscles;
- visceral pain from visceral nociceptors within body organs; it is generally difficult to localize and is described as cramping, achy, squeezing, or dragging.

The colonoscopy image demonstrates severe colitis that induced visceral nociceptive pain.

Neuropathic pain

- Neuropathic pain is pain induced by damage to the nerves themselves or by aberrant somatosensory pathways. Hyperpathic symptoms of burning, tingling, or electrical sensations are classic for neuropathic pain; other sensations include itching, stinging, squeezing, and numbness.
- Unfortunately, neuropathic pain is not traditionally responsive to standard pain medications;
- Multimodal therapy may be beneficial and includes psychotherapy, physical therapy, pharmacotherapy with antidepressants/anticonvulsants, and surgery.

- Herpes zoster (shown) can cause neuropathic pain via growth and inflammation within dermatomal nerves.

Pain Etiology

- Sympathetically mediated pain is accompanied by evidence of edema, changes in skin blood flow, abnormal pseudomotor activity in the region of pain, allodynia, hyperalgesia, or hyperpathia.
- Deafferentation pain is chronic and results from loss of afferent input to the CNS. The pain may arise in the periphery (eg, peripheral nerve avulsion) or in the CNS (eg, spinal cord lesions, multiple sclerosis).
- Neuralgia pain is lancinating and associated with nerve damage or irritation along the distribution of a single nerve (trigeminal) or nerves.

Pain Etiology

- Radicular pain is evoked by stimulation of nociceptive afferent fibers in spinal nerves, their roots, or ganglia, or by ectopic impulse generation. It is distinct from radiculopathy, but the two often arise together.
- Central pain arises from a lesion in the CNS, usually involving the spinothalamic cortical pathways (eg, thalamic infarct). The pain is usually constant with a burning, electrical quality. It is exacerbated by activity or changes in the weather. Hyperesthesia and hyperpathia and/or allodynia are invariably present, and the pain is highly resistant to treatment.

Pain Etiology

- Psychogenic pain is inconsistent with the likely anatomic distribution of the presumed generator, or it exists with no apparent organic pathology despite extensive evaluation.
- Referred pain often originates from a visceral organ. It may be felt in body regions remote from the site of pathology. The mechanism may be the spinal convergence of visceral and somatic afferent fibers on spinothalamic neurons. Common manifestations are cutaneous and deep hyperalgesia, autonomic hyperactivity, tenderness, and muscular contractions.

Sensitization

- Sensitization is an adaptive process in which innocuous stimuli produce an excessive response.
- Repeated intense stimuli to damaged tissue lower the activation threshold and increase the frequency of firing of afferent nociceptors.
- Local inflammatory mediators contribute by recruiting additional nociceptors, which normally remain silent to routine stimuli.
- Central sensitization may also be partly responsible for the pathophysiology of chronic pain syndromes.

- For example, patients with sunburns often experience intense pain and discomfort with even very light touch because of sensitization of the pain fibers.

The image illustrates the pain pathways involved in pain transmission and modulation (CGRP - calcitonin gene-related peptide; EAA - excitatory amino acids; GABA - gamma-aminobutyric acid; Gal - galanin; 5-HT - serotonin; NA - noradrenaline; NPY - neuropeptide Y; SP - substance P).

- *Image courtesy of Tavares and Martins.*

Pain modulation

- Pain modulation can both enhance and dampen pain signals.
- Placebo can have a significant analgesic response, and anxiety can magnify the perceived stimuli.
- Descending signals from the frontal cortex and hypothalamus help modulate the ascending transmission of the pain signal by opiate receptors.

Pain assessment

- Pain assessment should be ongoing, individualized, and documented.
- Patients should be asked to describe their pain in terms of the following characteristics: location, radiation, mode of onset, character temporal pattern, exacerbating and relieving factors, and intensity.
- It has been stated that the ideal pain measure should be sensitive, accurate, reliable, valid, and useful for both clinical and experimental conditions and able to separate the sensory aspects of pain from the emotional aspects.

Pain must be assessed using a multidimensional approach, with determination of the following:

- Chronicity
- Severity
- Quality
- Contributing/associated factors
- Location/distribution or etiology of pain, if identifiable
- Mechanism of injury, if applicable
- Barriers to pain assessment

Pain assessment. Chronicity of Pain

- Initial assessment of pain should always include the onset of pain and progression in time. Most clinicians and researchers use durations of either 3 months, 6 months.
- Recognizing the inception of pain may be crucial in determining its treatment. Onset of pain may be described as abrupt and sudden or insidious and gradual.
- Pain is said to be acute when presented within the first 3-6 months from the onset time. It typically has an abrupt start with identifiable associated events, although this may not be always true. It also may resolve within first 6 months without intervention.

Pain assessment. Chronicity of Pain

- Chronic pain does not resolve within 3–6 months of its initiation and progresses beyond 6 months of duration.
- Pain may also be described as constant, unrelenting, or intermittent. Symptoms may be most severe in the morning upon waking up, later in the day, or during the night, depending on the etiology of the pain. It is important to document whether the patient complains of disturbance in sleep secondary to the pain.

Pain assessment. Severity of Pain

- Pain is subjective expression. Objective quantification of pain has been one of the greatest challenges physicians have faced in modern medicine. There is obvious and great variability in the severity of pain among seemingly similar cohort groups. Several methods have been devised to measure pain.
- The measures presently available fall into two categories: single-dimensional scales and multidimensional scales. The numbers obtained from these instruments must be viewed as guides and not absolutes.
- The level of pain often fluctuates with activities of daily living, activity level, and work-related duties. Treatment of pain may be customized depending on the patient's physical activities and its presence at rest.

Pain assessment. Quality of Pain

- The quality of pain is described by the patient in purely subjective manner. Pain that is stimulated by nociceptive ending is usually characterized as:
- - thermal (eg, hot, cold),
- - mechanical (eg, crushing, tearing),
- - chemical (eg, iodine in a fresh wound, chili powder in the eyes).
- Another common quality of pain is attributed by its neuropathic origin. This pain is often described as burning, tingling, electrical, stabbing, or “pins and needles." It has its origin in the nervous system.

Pain assessment. Contributing/Associated Factors

- Nociceptive symptoms often can be amplified by certain body positions and/or activities. Frequently, patients complain of pain-inducing positions and activities that reduce quality of life in clinical settings.
- It is not uncommon to develop antalgic gait or positions in patients who deal with chronic pain. Furthermore, undertreated pain may lead to avoidance of movement, which in turn may cause muscle contractures and adhesive capsulitis.
- Psychogenic pain is inconsistent with the likely anatomic distribution of the presumed generator, or it exists with no apparent organic pathology despite extensive evaluation.

Pain assessment. Anatomical Etiology of Pain

- It is possible to describe different types of pain, and they tend to present differently. The history and physical examination help to identify these differences. Because the different types of pain tend to respond to different treatments, the identification of pain type during pain assessment is important.
- Referred pain often originates from a visceral organ. It may be felt in body regions remote from the site of pathology. The mechanism may be the spinal convergence of visceral and somatic afferent fibers on spinothalamic neurons. Common manifestations are cutaneous and deep hyperalgesia, autonomic hyperactivity, tenderness, and muscular contractions.

Pain assessment. Mechanism of Injury

- If applicable, the mechanism of injury can direct the clinicians in the correct path of diagnosis if there is trauma involved, especially if the symptoms are acute.
- Often, however, the mechanism of injury is due to repeated microtrauma over a long period of time. This type of injury may lead to degenerative, insidious, and chronic painful situations. At times, the mechanism of injury is not as obvious, such as with autoimmune diseases, mass effect from neoplastic process, and tissue damage from metabolic processes.

Pain assessment. Barriers to Pain Assessment

- Barriers to pain assessment occur because of the assessment's heavy reliance on subjective complaints. Pain assessment becomes even more complicated and difficult in patients who are nonverbal or have communication difficulties.
- Pain threshold is also an issue. There are two thresholds in terms of pain:
  - the perception threshold
  - the tolerance threshold.

Pain assessment. Barriers to Pain Assessment

- The pain perception threshold is the point at which the stimulus begins to hurt, and the pain tolerance threshold is reached when the subject acts to stop the pain. The variability of pain threshold is apparent not only in individual basis within one community, but it is also apparent between patients of different sex, ethnicity, and race.
- One of the most difficult challenges in chronic pain management is recognizing patients who are exaggerating their symptoms for secondary gains, including patients who abuse prescription opioids.

Pain assessment

- Determining the best treatment course for pain management begins with identification of the intensity and duration of the pain.
- Pain assessment relies largely upon the use of patient self-reports.

Pain measures fall into 2 categories:

- single-dimensional (rating pain intensity only)
- multidimensional scales are available.

Single-dimensional scales: These scales assess a single dimension of pain and, through patient self-reporting, measure only pain intensity; these scales are useful in acute pain when the etiology is clear. Examples of single-dimensional scales include:

- **the IASP Faces Pain Rating Scale, Revised**
- **the Numeric Rating Scale.**

Images courtesy of (top) IASP and (bottom) US Department of Veterans Affairs.

Multidimensional scales

- Multidimensional scales (eg, McGill Pain Questionnaire, Brief Pain Inventory) measure the pain intensity, the nature and location of the pain, and in some cases, the impact the pain is having on an activity or mood;
- multidimensional scales are useful in complex or persistent acute or chronic pain.
- The results obtained from these instruments must be viewed as guides, not absolutes.

- Although laboratory tests, imaging studies, and nerve or muscle conduction studies do not show pain in and of itself, these diagnostic modalities may help clinicians to identify the root cause of a patient's pain as well as provide important information for therapeutic planning.
- Knowing the cause of patients' pain and being aware of the extent of an injury may help clinicians and patients to select specific procedural or other therapeutic interventions to manage the underlying condition and alleviate pain.

- This sagittal MRI of a patient with lumbosacral radiculopathy demonstrates herniations of the nucleus pulposus at L4-L5 and L5-S1 that are responsible for the patient's pain symptoms.
- *Image courtesy of Barton Branstetter, MD.*

Medical management of pain proceeds in a stepwise fashion, as shown here (adapted from the WHO "pain ladder").

Pain management

- Acute pain is typically treated with short courses of pharmacotherapy, whereas chronic pain may require long-acting medications or other interventional modalities.
- For mild to moderate pain, nonnarcotic analgesics are used (eg, aspirin, acetaminophen, ibuprofen, naproxen, indomethacin, ketorolac);
- for moderate to severe pain, narcotic regimens are typically used (eg, codeine, oxycodone, morphine, hydromorphone, methadone, meperidine, fentanyl, tramadol).
- Combination regimens that contain opioids and nonnarcotic analgesics provide additive pain control.
- Adjuvant medications include tricyclic antidepressants, antihistamines, and anticholinergics.

Medication

1. Analgesics are commonly used for many pain syndromes. Pain control is essential to quality patient care. Analgesics ensure patient comfort, promote pulmonary toilet, and have sedating properties, which are beneficial for patients who have sustained traumatic injuries.

- **Oxycodone (OxyContin, Roxicodone)** is long-acting opioids may be used in patients with chronic pain. Start with a small dose and, if appropriate, gradually increase it.
- **Fentanyl (Duragesic, Fentora, Onsolis, Actiq)** is a potent narcotic analgesic with a much shorter half-life than morphine sulfate. It is the drug of choice for conscious-sedation analgesia.
- **Acetaminophen (Tylenol, FeverAll, Aspirin Free Anacin)** is the drug of choice for the treatment of pain in patients with documented hypersensitivity to aspirin or NSAIDs, with upper GI disease, who are pregnant, or who are taking oral anticoagulants.

Medication

2. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) have analgesic, anti-inflammatory, and antipyretic activities. Their mechanism of action is not known, but they may inhibit cyclo-oxygenase (COX) activity and prostaglandin synthesis. Other mechanisms may exist as well, such as inhibition of leukotriene synthesis, lysosomal enzyme release, lipoxygenase activity, neutrophil aggregation, and various cell membrane functions.

- **Ibuprofen (Motrin, Advil, Caldolor)** is the drug of choice for patients with mild to moderate pain. It inhibits inflammatory reactions and pain by decreasing prostaglandin synthesis.
- **Naproxen sodium** is used for the relief of mild to moderate pain.
- **Diclofenac** inhibits prostaglandin synthesis by decreasing COX activity, which decreases formation of prostaglandin precursors.
- **Indomethacin (Indocin)**
- **Ketoprofen** is used for relief of mild to moderate pain and inflammation. Small dosages are indicated initially in small patients, elderly patients, and patients with renal or liver disease. Doses higher than 75 mg do not increase the therapeutic effects.

Medication

3. Anticonvulsants. Certain antiepileptic drugs (eg, the gamma-aminobutyric acid [GABA] analogue gabapentin and pregabalin) have proven helpful in some cases of neuropathic pain.

- **Gabapentin (Neurontin)** has anticonvulsant properties and antineuralgic effects; however, its exact mechanism of action is unknown. It is structurally related to GABA but does not interact with GABA receptors.
- **Pregabalin** is a structural derivative of GABA; its mechanism of action unknown. Pregabalin binds with high affinity to the alpha2-delta site (a calcium channel subunit); in vitro, pregabalin reduces the calcium-dependent release of several neurotransmitters, possibly by modulating calcium channel function.
- Other anticonvulsant agents (eg, clonazepam, topiramate, lamotrigine, zonisamide, tiagabine) also have been tried.

Medication

4. Muscle spasmolytics are traditionally used to treat painful musculoskeletal disorders. As a class, they have demonstrated more CNS side effects than a placebo, sharing sedation and dizziness as common side effects.

- Benzodiazepines may be appropriate for concurrent anxiety states, and in those cases, clonazepam should be considered for its clinical use. Clonazepam is a benzodiazepine that operates via GABA-mediated mechanisms through the internuncial neurons of the spinal cord to provide muscle relaxation
- Nonbenzodiazepine: cyclobenzaprine, carisoprodol, methocarbamol, chlorzoxazone, and metaxalone
- Tizanidine is a central α-2 adrenoreceptor agonist that was developed for the management of spasticity due to cerebral or spinal cord injury

Medication

5. **Antidepressants.**

- Tricyclic antidepressants (TCAs) are commonly used in chronic pain treatment to alleviate insomnia, enhance endogenous pain suppression, reduce painful dysesthesia, and eliminate other painful disorders such as headaches. TCAs are used to treat both nociceptive and neuropathic pain syndromes. The presumed mechanism of action is related to the TCAs' capacity to block serotonergic uptake, which results in a potentiation of noradrenergic synaptic activity in the CNS's brainstem-dorsal horn nociceptive-modulating system.
- Little evidence supports the use of SSRIs to attenuate pain intensity, and studies have suggested that these agents are inconsistently effective for neuropathic pain at best

The pharmacology of pain control hinges on influencing one of several biochemical pathways.

- Many nonnarcotic analgesics inhibit cyclooxygenase, the enzyme that is responsible for the formation of prostaglandin, prostacyclin, and thromboxane.
- Opiate medications mimic endogenous opioid peptides.
- Opioids bind to one of three principal classes of opioid receptors (mu, kappa, delta) to produce centrally mediated analgesia.
- Tricyclic antidepressants are thought to potentiate the effect of opiates.

Image of a PCA infusion pump configured for epidural administration of fentanyl and bupivacaine for postoperative analgesia *(courtesy of Wikimedia Commons).*

- Patient-controlled analgesia (PCA) allows patients to self-titrate their intravenous pain medication.
- This method of pain control also allows more consistent administration of analgesia and shortens the interval between when the patient feels pain and when the analgesia is administered. PCA reduces the chances for medication errors, reduces nursing workload, increases patient autonomy, and provides objective data about the amount of medication a patient needs. It is traditionally used for postoperative patients and those with serious oncologic or hematologic diseases.

Transdermal patches provide controlled drug delivery with a lower potential for abuse than is present with oral analgesics, a lower risk of adverse effects, and a reduction in the frequency of dosing. This form of drug delivery also includes the potential for skin reactions, a delayed onset of action, and a decrease in drug delivery from the loss of adhesive properties. Transdermal patches are routinely used to treat conditions such as postherpetic neuralgia and chronic cancer pain. The patches can be applied once every 12-24 hours. Alternative forms of drug delivery used to treat patients with malignant pain include opiate-infused lollipops and buccal lozenges.

Image courtesy of Lisa Wong, RPh.

The image shows a patient undergoing a sural nerve block.

Regional anesthesia with therapeutic injections can provide excellent relief for patients with localized pain and inflammation. Depending on the clinical scenario, nerve blocks may be used for therapeutic, sympathetic, diagnostic, prognostic, or prophylactic purposes.

E.g., therapeutic injections permit a return to normal function by preventing the development of compensatory injuries. The exact procedural technique is dependent on the nerve involved, but the general principle involves the direct injection of a local anesthetic or corticosteroid into the perineural space.

Depending on an operator's familiarity and the difficulty of accessing injection sites, image guidance may be used for direct visualization. This computed tomography – guided image demonstrates an injection needle at L5 for a transforaminal nerve block, which can be performed for the diagnosis and treatment of radicular pain. CT, ultrasonographic, and fluoroscopic guidance allow more precise needle placement, thus decreasing the amount of injected drug and reducing the risk of complications. The technique is especially useful in patients with distorted native anatomy.

Image courtesy of Frank Gaillard, MBBS, MMed, FRANZCR, at Radiopaedia.org.

- Surgical interventions are generally limited to patients with discrete deficits whose condition does not improve with conservative management. Depending on the location of pain, patients will typically undergo a stepwise treatment course involving noninterventional management before being eligible for invasive therapy. Surgically implanted devices, such as intrathecal pumps (shown) and spinal cord stimulators, are available for use on a case-by-case basis.

Image of an intrathecal baclofen pump and associated tubing (as well as separate tubing from a ventriculoperitoneal shunt) in a patient with hydrocephalus and new-onset nausea and pain

Courtesy of Yuranga Weerakkody, MBChB, FRANZCR, at Radiopaedia.org.

Spinal cord stimulation (SCS) is approved by the US FDA to relieve intractable pain. Indications include failed back surgery syndrome, chronic painful peripheral neuropathy, complex regional pain syndromes, and intractable low back pain. SCS may also be considered for postherpetic neuralgia. The neurophysiologic mechanisms of SCS are not completely understood. Experimental evidence supports a beneficial SCS effect at the dorsal horn level, whereby the hyperexcitability of wide-dynamic-range neurons is suppressed. Evidence also exists for increased levels of GABA, serotonin, substance P, and acetylcholine.

Image of a spinal cord stimulator implanted in the posterior epidural space of the thoracic spine courtesy of Wikimedia Commons.

A transcutaneous electrical nerve stimulation (TENS) unit is an adjuvant pain control device that provides pulsatile low-voltage electric impulses. The proposed mechanisms by which TENS reduces pain are presynaptic signal inhibition, endogenous pain control, direct inhibition of abnormally excited nerves, and restoration of afferent inputs. This method of pain control has been used for low back, arthritic, sympathetically mediated, neurogenic, visceral, and postoperative pain. Although TENS is widely used and there is a great deal of anecdotal and observation-based evidence, there remains a paucity of randomized controlled trials confirming the effectiveness of this modality.

Image courtesy of Wikimedia Commons.

Chronic, refractory pain is best managed with a multidisciplinary team approach that includes psychology, occupational therapy, physical therapy, osteopathic manipulative treatment, vocational rehabilitation, and relaxation training.

Patients with chronic pain frequently seek complementary and alternative medicine treatment options as well, including acupuncture, dietary supplements, and hypnosis.

Image courtesy of Wikimedia Commons.