

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. This implies that pain has not only physical attributes but also a strong psychological component. Keeping this in mind there has been emphasis on the biopsychosocial approach to the diagnosis and management of chronic pain conditions. It is generally agreed that any pain lasting more than three months is considered chronic pain.

As many as 15 to 25% of general adult population world over suffer from chronic pain. Although epidemiological studies of chronic pain in India are limited, there is no reason to believe that the figures for India would be any less. One study pegs the point prevalence of chronic pain in India at around 15%, i.e one in six adults. Furthermore, in India, two thirds of people with chronic pain reported their pain to be of severe nature, and a third of these patients reported to have lost at least 4 hours of work in the preceding three months due to pain<sup>1</sup>. These numbers are a good gauge of the huge economic impact of chronic pain - both at personal and societal levels.

Although it is agreed that all pains must be treated effectively, there is still a marked reluctance in using the vast armamentarium of drugs available to ease pain. This is to show a blind eye to the enormous benefits of treating pain well. Some of the physical benefits of meticulous pain management include improved sleep, better appetite, early mobilisation, faster recovery after injury/surgery, and fewer associated complications such as myocardial ischemia, pneumonia and deep vein thrombosis. Good pain relief results in faster discharge from hospital and lesser readmission rates thereby positively impacting the cost of healthcare. Well treated pain, in addition, means lesser anxiety and depression; and optimal pain reduction not only helps the sufferer but also his/her family and society. A relatively pain free person functioning well as part of the family and also providing for it, in turn, contributes to the community.

### CLASSIFICATION

Appropriate treatment of pain depends on our ability to identify the type of pain that afflicts the patient. Although there are numerous ways of classifying pain, a simple method would be:

1. Based on the duration of pain
  - a. Acute pain (pain of less than 3 months duration)
  - b. Chronic pain (pain lasting for more than 3 months)

On occasions, a patient with chronic pain may develop an acute exacerbation where it might be viewed as acute on chronic pain eg: acute flare up in chronic pancreatitis and pathological fracture in bony metastasis.

2. Based on etiology
  - a. Cancer pain: pain in cancer is progressive more often than not, and is of chronic nature. Acute exacerbations are not uncommon.
  - b. Non cancer pain: Surgery, headaches, osteoarthritis, labour pain, burns, nerve compression/neuropathy are a few causes of non cancer pain. It can be acute, chronic or acute on chronic.
3. Based on neural mechanism
  - a. Nociceptive pain - caused by stimulation of pain receptors in injured tissue.
  - b. Neuropathic pain- caused by damage to or abnormal function of nervous system.

### PATHOPHYSIOLOGY OF PAIN

Here, let us describe the major characteristics of and differences between nociceptive and neuropathic pain, and the peripheral and central mechanisms driving them.

**Nociceptive pain :** Pain is termed such when the clinical evaluation suggests that it is sustained primarily by the nociceptive system. It is proportionate to the degree of actual tissue damage i.e. a more severe injury results in pain that is perceived to be greater than that caused by a less severe injury. Such pain serves a protective function and influences behaviours that reduce injury and promote healing e.g., pulling the hand away from a hot object. Other examples of nociceptive pain include acute burns, bone fracture, and other somatic and visceral pains.

**Neuropathic pain :** Unlike nociceptive pain, neuropathic pain occurs due to peripheral nervous system (PNS) changes, such as neuroma formation, ectopic discharge from the injured axons or the somata of the dorsal root ganglion (DRG) neurons, or through central nervous system (CNS) changes that can lead to enhanced excitability of central pain networks (termed central sensitization) in patients with a prolonged exposure to noxious stimuli or nerve injury. It is disproportionate to the degree of tissue damage and can persist in the absence of continued noxious stimulation (i.e., the pathophysiologic changes become independent of the inciting event). Neuropathic pain, therefore, serves no protective function and provides no benefit to the overall

## Differences between Nociceptive Pain & Neuropathic Pain

Nociceptive Pain	Neuropathic Pain
<ul style="list-style-type: none"> <li>• Warns of acute or potential tissue damage</li> <li>• Has protective functions</li> <li>• Can be differentiated from touch</li> <li>• Transient</li> <li>• Well localized</li> <li>• C and A<math>\delta</math> fiber mediated</li> <li>• Increased activity, Wide dynamic Range Neurons</li> <li>• Opioid sensitive</li> </ul>	<ul style="list-style-type: none"> <li>• Pain caused by nerve injury</li> <li>• Could be spontaneous or evoked</li> <li>• Develops in days or months</li> <li>• Associated with inflammation &amp; neuropathy</li> <li>• Associated with peripheral and central sensitisation</li> <li>• Pain outlasts duration of the stimulus</li> <li>• Pain sensed in non injured areas</li> <li>• Elicited by A<math>\beta</math> as well as C and A<math>\delta</math> fibers</li> <li>• Opioid insensitive</li> </ul>

health of the person. This table compares and contrasts the salient features of nociceptive and neuropathic pain.

### A BRIEF NOTE ON THE NOCICEPTIVE PATHWAY

A knowledge of the pathways that mediate nociception under normal conditions would help us better understand the pathophysiology of abnormal or neuropathic pain. The first step in nociception is the transduction of the sensory stimulus into an electrical potential by first-order afferent neurons in the DRG located external to the spinal cord. These neurons express specialized receptors at their distal ends that respond to specific types of sensory stimuli - external (e.g. the skin) or internal (e.g. visceral organ like the liver) - by opening ion channels in their membrane. The depolarization of the sensory neuron then triggers an action potential that propagates to the dorsal horn of the spinal cord. Noxious stimulation is transmitted via small-diameter DRG neurons that give rise to either thin myelinated A $\delta$  fibers (which conduct impulses at 2-30 m/sec) or small unmyelinated C-fibers (with conduction velocities of < 2 m/sec). Large-diameter DRG neurons possess large myelinated axons with rapid conduction velocities in the A $\beta$  range (>30 m/sec) and generally transmit information about innocuous mechanosensation (e.g. touch, vibration).

The signals carried by all three types of sensory afferents are integrated by the synaptic network within the spinal dorsal horn, which consists of both local circuit interneurons and second-order projection neurons that transmit impulses from the spinal cord to higher brain areas (including the thalamus) predominantly via the spinothalamic tract (STT). The output of these STT neurons depends on the net balance between inhibitory and facilitatory mechanisms within the dorsal horn.

The activation of third-order neurons in the thalamus by STT inputs allows the transmission of the noxious information to the somatosensory cortex, where nociception occurs. Numerous supraspinal control areas—including the reticular formation, midbrain, thalamus, hypothalamus, the limbic system of the amygdala and the cingulate cortex, basal ganglia, and cerebral cortex—appear to modulate the sensation of pain. It is useful to observe here that pain is a personal experience influenced by multiple factors, whereas nociception is only its neural

correlate.

### PERIPHERAL AND CENTRAL MECHANISMS OF NEUROPATHIC PAIN

The mechanisms underlying neuropathic pain involve both peripheral and central components. A combination of these mechanisms results in the phenomenology of pain that could be spontaneous or evoked. The later manifests as hyperalgesia (exaggerated response to a painful stimuli) or allodynia (a non-noxious stimuli resulting in a painful response).

#### PERIPHERAL MECHANISMS

1. Altered expression of ion channels in axotomised neurons: There is now compelling evidence that the expression of sodium channel subtypes (e.g., Nav1.3, Nav1.7, Nav1.8, and Nav1.9) are dramatically altered by nerve injury and may account for the increased excitability of neuropathic DRG neurons in models of chronic pain. Changes in the expression of potassium and voltage gated calcium channels have also been demonstrated in chronic pain models.
2. Sympathetic excitation of injured sensory neurones: In certain pain conditions like post herpetic neuralgia and complex regional pain syndromes (CRPS) abnormal coupling between sympathetic and the sensitised nervous system maintain what is sometimes referred to as sympathetically mediated pain. It manifests clinically as oedema, sweating, and changes in skin colour and temperature.
3. Inflammatory cytokines and chemokines: Proinflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin (IL)-1 and IL-6, and chemokines have profound effects on neuronal activity and pain sensitivity.

#### CENTRAL (SPINAL AND SUPRASPINAL) MECHANISMS

1. Long term potentiation of nociceptive inputs in dorsal horn of spinal cord: Strong activation of nociceptive sensory afferents can lead to a greater synaptic drive onto spinal projection neurons and a subsequent facilitation of pain transmission from the spinal cord to the brain.

2. **Loss of central inhibition:** Reductions in the efficacy of GABAergic and glycinergic transmission allow for greater firing in the spinothalamic tract output cells.
3. **Spinal glial activation:** There is now significant evidence showing that glial activation in the spinal cord appears to be important for both the initiation and the maintenance of pathologic pain. Astrocytes and microglia are activated by neuronal signals including substance P, glutamate, and fractalkine
4. **Supraspinal pain modulation:** Descending connections between higher centres of the brain and the spinal cord can either amplify or inhibit the transmission of pain related signals. Mounting evidence suggests that these descending systems are involved in the maintenance of neuropathic pain. Peripheral nerve injury results in the strengthening of the descending facilitatory pathways from the rostral ventral medulla, producing an enhanced excitability of the dorsal horn and a subsequent increase in the sensitivity to pain<sup>2</sup>.
6. **Exacerbating/Alleviating factors:** This refers to pain modifiers noticed by the patient. Exacerbation of back pain by spinal movement or loading is a typical example

The past medical history could be important for several reasons. Serious comorbidities may complicate or even contraindicate some pain treatment options. Particular hazards of systemic drug treatments may be posed by seriously impaired liver or kidney function, and some invasive treatments carry greater risk in patients with an increased bleeding tendency, either from a hemorrhagic disorder (e.g. thrombocytopenia, hemophilia) or anticoagulant treatment. Treatment history including both pharmacological and non pharmacological treatment, especially medications tried, dosage, duration and the reason for their discontinuation are useful. And so are details of non pharmacological treatments like surgery, acupuncture, alternative medicines, exercise therapy and electrotherapy.

An appropriate starting point for psychosocial history are the patient's personal circumstances (who else are at home? are you working? what is your job?). It is useful to explore the effect of the pain on activity and behavior in domains such as occupational, domestic, social, recreational, and sexual. Also important is the history of its impact on emotions (anxiety, depression, anger, frustration). On many occasions, they might have already consulted a mental health professional.

The physical examination starts with observing for pain-related behaviours such as gait, use of secondary aids and facial expression. A vast majority of chronic pains have their origin in, or influence, the musculoskeletal and the nervous system.

Key features of musculoskeletal examination include:

- Stigmata of specific rheumatological disease, e.g. osteoarthritis
- Abnormalities of posture/gait, and fixed deformity
- General level of fitness
- Scars of previous surgery
- Abnormalities of skin and subcutaneous soft tissue
- Range of movement of affected joint or spine.
- Antalgic movements and distress behaviour
- Local tenderness and myofascial tender points
- Straight leg raise: Reduced straight leg raise is generally regarded as having high sensitivity for lumbar disk herniation but poor specificity
- Sacroiliac joint (SIJ) stressing tests for buttock pain

Key features of examination in patients with neuropathic pain<sup>3</sup>:

- abnormalities of posture or gait
- abnormal involuntary movement

### EVALUATION OF A PATIENT WITH CHRONIC PAIN

As in any branch of medicine the physician-patient interview is the most important part of assessment. It is useful to ask the chronic pain patient, at some point, about their expectations with the consultation. Some expect a diagnosis (or a test that will lead to diagnosis) while others might want their pain to be relieved. Some have unrealistic expectations of what is achievable and we should be alert about it early on. It is a useful exercise to allow the patient to narrate his/her story in their own words rather than providing them with leading questions. This allows the patient to talk about problems which are most important to them and to feel "listened to". When the patient has completed telling their story of the main complaint, we can then fill in the gaps in history and explore relevant symptoms in more detail by applying a more traditional "doctor-centered" interviewing technique.

The following aspects could be noted in the context of establishing a diagnosis

1. **Location:** It may be helpful to ask the patient to indicate the site and extent of the pain on a body line-drawing. In some conditions, the diagnosis may be made with near certainty on the basis of this alone, for example meralgia paresthetica
2. **Onset**
3. **Intensity**
4. **Temporal pattern :** Pain that is unremitting is often neuropathic. In addition, if there is not much variation and it is rarely influenced by physical activities it may suggest a central origin
5. **Quality:** Shooting, electrical, or burning sensations are characteristic of neuropathic pains, while nociceptive pains are more likely to be described as aching, dull, cramping, or throbbing.

- 442
- focal wasting
  - local changes of colour or swelling
  - locally altered temperature/sweating
  - tone, power, reflexes in the motor assessment
  - light touch – deficit/allodynia
  - warm/cool – deficit/allodynia
  - pinprick – deficit/hyperalgesia
  - proprioception/vibration
  - movement- or pressure-evoked sensation (if appropriate to presentation) – e.g. Tinel’s test (paresthesia in the hand/fingers provoked by percussion over the median nerve at the wrist in carpal tunnel syndrome).

A psychological evaluation would help

- to determine the degree of psychological adaptation to chronic pain which includes mood state, coping skills, effect on family, and especially level of physical functioning
- to evaluate the patient’s premorbid psychological state and personality factors and its effect on onset and etiology of pain
- to establish the role of psychological factors in the etiology, maintenance, and exacerbation of pain
- to devise a treatment plan in conjunction with the patient and the rest of the multidisciplinary team
- to predict outcome of invasive medical procedures

Various questionnaires (McGill Pain Questionnaire, Beck’s Depression Inventory, Minnesota Multiphasic Personality Inventory, Coping Strategies Questionnaire) are available to assess the psychology of patients with chronic pain<sup>4</sup>.

### COMMON CHRONIC PAIN CONDITIONS AND MANAGEMENT

It is beyond the scope of this article to discuss in detail all chronic pain syndromes and their treatment options. Only an overview is provided.

### HEADACHE & FACIAL PAINS

Trigeminal Neuralgia: Carbamazepine, oxcarbamazepine, phenytoin, gabapentin, pregabalin and baclofen are the drugs commonly used for pain relief. Despite excellent short-term response to carbamazepine, long-term pain relief is often not maintained. Retrogasserian percutaneous radiofrequency thermocoagulation is a technique of controlled thermal ablation of nerve fibers in the trigeminal ganglion or nerve root that relieves pain<sup>5</sup>.

Cluster headache: Sumatriptan, zolmitriptan and 100% oxygen have been used as abortive therapies. Verapamil, prednisolone, lithium, ergotamine, methysergide and indomethacin are useful as preventive medications. Sphenopalatine ganglion radiofrequency thermocoagulation and trigeminal ganglion thermocoagulation are percutaneous interventions

that are effective in relieving pain that is resistant to medications.

Occipital neuralgia: Occipital neuralgia causes pain in the distribution of the greater or lesser occipital nerves or of the third occipital nerve, sometimes accompanied by diminished sensation or dysesthesia in the affected area. The pain is often deep or burning, with superimposed paroxysms of shooting pain. Anesthetic blockade of the nerve temporarily reduces or abolishes the pain. Long-term peripheral neurostimulation may be a safe and relatively effective method for the treatment of intractable occipital neuralgia.

### NECK PAINS

The treatment of neck pain is as varied as its etiology, with a choice of pharmacological, physical, interventional injection, and surgical techniques. Soft tissue and cervical spine disease are the most common causes of neck pain. Soft tissue structures include fascia, ligaments, tendons, and muscles. Disorders of the synovial joints and intervertebral discs of the cervical spine may contribute to neck pain as well as refer pain into the posterior head, the shoulder, and distally into the arm. Pharmacotherapy includes NSAIDs, anticonvulsants (pregabalin, gabapentin), anti depressants (amitriptyline, duloxetine), opioids (tramadol, tapentadol, buprenorphine). Interventional techniques in vogue are trapezius, rhomboid and splenius myofascial trigger point injections. Epidural steroid injections for cervical radiculopathy provides satisfactory pain relief. Facetogenic pain is treated with radiofrequency denervation of the zygapophyseal joints<sup>6</sup>. All these interventional treatments are followed up with aggressive rehabilitation.

### LOW BACK ACHES

A majority of back pains are myofascial in nature and resolve spontaneously. However there exists a significant population where low back ache and lower limb radicular pain becomes chronic. More than a dozen pain generators have been identified in the spine and surrounding musculature. Interspinous ligaments, paraspinal muscles, quadratus lumborum, intervertebral disc, facet joints and their coverings, sacroiliac joint, piriformis muscle, nerve roots, the vertebrae could all cause pain. Thorough clinical evaluation in conjunction with appropriate imaging is needed to diagnose the pain generator. While pharmacological management is similar to neck pain, myofascial trigger point injections, caudal epidural, interlaminar epidural, transforaminal epidural, lumbar facet denervation, SIJ denervation, piriformis myofascial injection, dorsal root ganglion pulsed radiofrequency ablation are some of the interventions offered for low backache. Advanced interventions include spinal cord stimulators for post laminectomy syndrome with leg pain. As with neck pain, subsequent rehabilitation is important to achieve better outcomes.

### SHOULDER PAIN

The shoulder joint could be a common cause for pain. Adhesive capsulitis, osteoarthritis, supraspinatus

tendinitis, biceps tendinitis, and acromio-clavicular joint afflictions are the most common. When conservative measures, including medications, physiotherapy and exercises fail, ultrasound guided glenohumeral joint injection, biceps peritendon infiltration, subdeltoid bursa infiltration, suprascapular nerve blocks and pulsed radiofrequency ablation, and acromioclavicular joint injections are common procedures to achieve pain relief. Range of movement exercises and other specific exercises for the specific condition are necessary after the procedures.

### KNEE PAIN

Osteoarthritis knee is extremely common in middle and older aged people. Rehabilitation in consultation with physiotherapy is vital. Lifestyle modification also plays a vital role in alleviating pain. Early stages of osteoarthritis can be managed with genicular nerve radiofrequency ablations. This gives meaningful benefit and can help in postponing the need for surgery.

Other miscellaneous musculoskeletal issues amenable to interventions include plantar fasciitis, tennis and golfers elbow, Dequervain tenosynovitis, carpal tunnel syndrome to name a few.

### CANCER PAIN

The incidence of new cancer patients in India is around 10 lakh every year. One third of these patients have pain at diagnosis. This increases to two thirds of the patients having pain in the advanced stage. Amongst the patients having pain, one third have a single pain and two thirds have two or more pains. More than 75% of pains can be treated effectively using the WHO analgesic ladder. In reality, due to patient related, physician related and healthcare system related barriers adequate pain relief is not extended to these patients. Pharmacotherapy of cancer pain involves stepwise use of NSAIDs, weak opioids and strong opioids like morphine and fentanyl - what is commonly referred to as WHO analgesic ladder. Other adjuvants like anti emetics, anti spasmodic, sedatives, antacids, antibiotics, anti depressants, anticonvulsants are necessary to achieve optimal patient comfort. Celiac plexus neurolysis (for abdominal malignancies), superior hypogastric plexus neurolysis (for pelvic malignancies), ganglion impar neurolysis (for primal malignancies), Intrathecal morphine therapy, intrathecal neurolysis using alcohol or phenol are some of the commonly used interventions to relieve cancer pain.

### NEUROPATHIC PAIN

The etiology of neuropathic pain could be traumatic (spinal cord injury), metabolic (painful diabetic neuropathy), viral (postherpetic neuralgia), surgical (post-hernia repair pains) or drug-induced (chemotherapy-induced neuropathy). The diagnosis of neuropathic pain is made when:

1. Pain distribution is neuroanatomically plausible
2. History is suggestive of relevant lesion or disease
3. Sensory signs : negative or positive signs within

innervations territory of lesion are present

4. Diagnostic test confirms a lesion or disease

The first line drugs in the management of neuropathic pain are gabapentinoids (gabapentin and pregabalin), serotonin and noradrenaline reuptake inhibitors (duloxetine, venlafaxine) and tricyclic antidepressants (amitriptyline). The second-line drugs include tramadol and lidocaine patches. A combination of medications is normally required to achieve the desired benefit<sup>7</sup>.

### MULTI DISCIPLINARY APPROACH TO PAIN MANAGEMENT

Patients with chronic pain (especially chronic non cancer pain) often require long term care with frequent reassessment and adjustment of therapy. The biopsychosocial model of chronic pain recognises the condition as a combination of physical dysfunction, beliefs and coping strategies, distress, illness behaviour and social interactions. The multitude of factors that contribute to chronic pain often means that the condition fails to respond well to a single treatment approach. In order to achieve better outcomes in terms of analgesia and quality of life, a range of specialist treatments administered by a multi disciplinary team and tailored to the individual patient's needs are necessary. The core members of the team vary according to local factors but typically consist of primary care physician, pain physician, psychiatrists, psychologists, physiotherapists and nurses. Numerous studies have shown a favourable outcome with multidisciplinary pain management programs in terms of both patient satisfaction and the economics of chronic pain<sup>8</sup>.

### REFERENCES

1. Dureja G. P., Jain P. N., Shetty N., et al. Prevalence of chronic pain, impact on daily life, and treatment practices in India. *Pain Practice*. 2014; 14:E51-E62. doi: 10.1111/papr.12132.
2. Jun-Ming Zhang, Mark L. Bacei. Pathophysiology of pain. Howard Smith. Current therapy in pain. 1<sup>st</sup> Ed. Philadelphia: Saunders Elsevier; 2009.
3. Paul R Nandi, Toby Newton. History taking and examination of the patient with pain. Harald Breivik. Clinical pain management practice and procedures. 2<sup>nd</sup> Ed. London: Hodder & Stoughton Limited; 2008.
4. Allen H Lebovits. The psychological assessment of patient with chronic pain. Peter R Wilson. Clinical Pain Management Chronic pain. 2<sup>nd</sup> Ed. London: Hodder & Stoughton Limited; 2008.
5. Andrew Linn, Zahid H Bajwa. Trigeminal Neuralgia. Howard Smith. Current therapy in pain. 1<sup>st</sup> Ed. Philadelphia: Saunders Elsevier; 2009.
6. Susan Elizabeth Opper. Neck pains. Howard Smith. Current therapy in pain. 1<sup>st</sup> Ed. Philadelphia: Saunders Elsevier; 2009.
7. Nanna Finnerup et al. Pharmacotherapy of neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurology* 2015; 14:162-173.
8. <http://www.pae-eu.eu/wp-content/uploads/2013/12/Multidisciplinary-approach-in-chronic-pain-management.pdf>.