Pain Module

Neuropathic Pain
Defining Neuropathic Pain

- The International Association for the Study of Pain: ‘pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation in the peripheral or central nervous system’. In other words, it is pain caused by damaged or dysfunctional nerves in the periphery, spinal cord or brain.

- Neuropathic pain is not one single disease but constitutes a heterogeneous group of diseases and lesions that produce a common syndrome characterized by pain within a territory that has lost its normal afferent input to the CNS. The neuropathic pain syndrome is one among several other conditions resulting in long-lasting pain. An essential element in neuropathic pain is the combination of sensory loss and the paradoxical presentation of hypersensitivity in the painful area.

- The end result is pain that is experienced without evidence of a continuing noxious stimulus.
Classification of Neuropathic Pain by Pathology

• **Peripherally Generated**
  
  – Painful polyneuropathies
    • Pain resulting from toxins, drugs, metabolic & autoimmune diseases, that is felt along many nerve distribution sites e.g., diabetic neuropathy.
  
  – Painful mononeuropathies
    • Pain felt along the damaged nerve e.g., carpal tunnel, sciatica.

• **Centrally Generated**
  
  – Deafferentation pain
    • Injury in the CNS or the peripheral system resulting in loss of sensory input into the central nervous system e.g., phantom limb pain—the injury was peripheral, but the CNS is generating signals that the brain perceives are coming from the limb that is missing.
  
  – Sympathetically maintained pain
    • Associated with dysregulation of the autonomic nervous system e.g., complex regional pain syndrome, usually following trauma to the area. Pain is often described as severe burning pain with allodynia and hyperpathia. Signs of sympathetic overactivity include increased color changes, sweating, & cold skin of the affected area.
Neuropathic pain syndrome is characterized by:

- Pain in a neuroanatomical area with partial or complete sensory loss.
- Pain can occur spontaneously or as a result of exposure to mildly painful stimuli (hyperalgesia) or stimuli not normally perceived as painful (allodynia).
- Aftersensations (pain outlasting the period of stimulation).
- Abnormal summation of pain (increased pain following repetitive stimulation).
- Neuropathic pain often is described as burning, shooting, stabbing, paroxysmal, or electrical, raw skin, deep, dull, bonelike ache.
- The sensations caused by nerve damage evoke vivid descriptions by patients when asked to describe what the pain feels like.
Definitions related to neuropathic pain

• Causalgia--A syndrome of sustained burning pain, allodynia, and hyperpathia, often combined with vasomotor and sudomotor dysfunction and later trophic changes.
• Neuralgia--Pain in the distribution of a nerve or nerves.
• Dysesthesia--An unpleasant abnormal sensation, whether spontaneous or evoked.
• Allodynia--pain elicited by a normally nonnoxious stimulus (clothing, air movement, touch, cold or warmth).
• Hyperalgesia--exaggerated pain response to a mildly noxious (mechanical or thermal) stimulus
• Hyperpathia--delayed and explosive pain response to a noxious stimulus
• Central sensitization is abnormal hyperexcitability of neurotransmitters mainly in the dorsal horn of the spinal cord. Peripheral nerve damage, with its resulting barrage of nerve signals being sent along the pain pathways to the CNS system can result in neuroanatomic, neurophysiologic, and/or neurochemical changes resulting in central sensitization.
Some Causes of Neuropathic Pain

Pain is sustained by abnormal processing of stimuli from the peripheral nervous system or central nervous system or both. Damage to the somatosensory nervous system represents a potential risk for the development of neuropathic pain e.g.,

- hereditary abnormalities
- plexopathies (caused by nerve compression, e.g., carpal tunnel, neuroma, tumor, or herniated disk)
- neuropathies due to metabolic disorders such as diabetes
- diseases of the CNS such as stroke and multiple sclerosis
- traumatic nerve injury from accidents or surgery
- viral infections e.g., HIV, shingles
- neuropathy due to immuno-globulinemias and demyelinating inflammatory disorders e.g., rheumatoid arthritis, systemic lupus erythematosus, Sjögren’s syndrome
- toxins (ciguatera poisoning, alcohol, several chemo drugs)
- dietary or absorption abnormalities
Examples of Neuropathic Pain

- Lower back pain, acute and chronic
- Post-traumatic pain syndrome
- Chronic abdominal and pelvic pain
- Acute herpes zoster, shingles, post-herpetic neuralgia
- Atypical facial pain/trigeminal neuralgia
- Neck pain, acute and chronic
- Cancer pain, focal or generalized
- Pain associated with surgical incisions
- Chest wall pain, acute and chronic
- Rib fractures
- Diabetic and systemic neuropathy
- Myofascial pain syndromes
- Peripheral vascular insufficiency/ischemic pain
- Post-laminectomy syndromes/arachnoiditis
- Post-stroke and central pain syndromes
- Raynaud's syndrome
- Spinal cord injury pain syndromes
- Stump and phantom limb pain
- Sympathetically mediated pain
- Peripheral entrapment neuropathies/neuromas
- Complex Regional Pain Syndrome (CRPS).
Diagnosing Neuropathic Pain

• History and clinical examination.
• Validated clinical screening tools and questionnaires that identify neuropathic components, and assess the different types of neuropathic pain may be helpful.
• Certain lab tests may be helpful e.g., Lyme titers, hepatitis B and C, HIV screening, antinuclear antibodies, rheumatoid factor, Sjögren’s titers & others.
• Cerebrospinal fluid study for demyelinating diseases and meningeal carcinomatosis.
• EMG and/or quantitative sensory testing may be useful for assessing nerve pathway dysfunction, and skin biopsy for assessing neuropathies with distal loss of unmyelinated nerve fibers.
Treatment

• The elimination of the causative agent is rarely possible, and symptomatic treatment of the pain is often the best that can be done.

• Neuropathic pain remains a major clinical problem and a therapeutic challenge because existing analgesics are often ineffective and can cause serious side effects.

• Referral to a specialist in this field is essential, because these individuals may be their only hope for relief.

• Despite these efforts, 66% of patients do not get sufficient pain relief from current treatments and are left to deal with terrible, chronic pain which interferes with their quality of life.
Treatments—Interventional and Medications

- **Interventional approaches** e.g., nerve blocks (epidural, facet, IV regional, sympathetic); nerve ablation via radiofrequency, electrocoagulation or neurolytic blocks; intraspinal via injections of opioids, local anesthetics, steroids, and/or baclofen; implantable pain pumps, spinal cord stimulators (see module on Interventional Approaches).

- **Medications**—The drug classes for which there is the best evidence for a clinical relevant effect are:
  - Tricyclic antidepressants,
  - serotonin noradrenaline reuptake inhibitors
  - anticonvulsants especially gabapentin and pregabalin
  - opioids
  - topical lidocaine and capsaicin may be helpful for some.
  - NMDA antagonists may be helpful for centrally generated pain.

- The above meds act on the nervous system by
  - Interactions at cell surface receptor sites or membrane ion channels, or
  - Alteration of synaptic neurotransmitter levels

- There are no exact data that permit presentation of a treatment algorithm for all types of neuropathic pains. In practice, treatments are often combined, but at present, there are limited controlled trials documenting the efficacy of combination therapies. The best available one is a combination of opioids and gabapentin. Tramadol may be helpful for painful polyneuropathies.

- Botulinum toxin may be helpful for certain types of neuropathic pain.
Sites where various medications work in the nervous system

- **BRAIN**
  - Descending Modulation
    - Anticonvulsants
    - Opioids
    - Tricyclic/SNRI Antidepressants

- **CNS**
  - Central Sensitization
    - Anticonvulsants
    - Opioids
    - NMDA-receptor Antagonists
    - Tricyclic/SNRI antidepressants

- **Spinal Cord**
  - Local Anesthetics
  - Topical Analgesics
  - Anticonvulsants
  - Tricyclic Antidepressants
  - Opioids

- **PNS**
  - Peripheral Sensitization