CHAPTER

1

Pain

Definition

According to the International Association for the study of pain, pain is defined as "an unpleasant feeling often caused by intense or damaging stimuli".

Sherrington defined Pain as the psychical (pertaining to the mind) adjunct (joined to) of an imperative (urgent) protective reflex.

TYPES OF PAIN

Pain can be classified as:

1. Somatic and visceral pain
2. Fast and slow pain
3. Acute and chronic pain
4. Psychological pain

Somatic and Visceral Pain

- **Somatic pain:** Pain derived from the stimulation of the cutaneous and subcutaneous receptors. It is sharp and well localized. Localization is based on the quantity of the skin innervations with receptors. It leads to reflex withdrawal movements, increase in heart rate, blood pressure and respiration. This pain does not radiate.
- **Visceral pain:** Pain derived from the stimulation of visceral receptors. The pain is dull and poorly localized, because of a few receptors and 'A' delta fibers. Sometimes this pain produces faintness, nausea, vomiting, sweating, bradycardia and low blood pressure. It is both local and radiates to different areas.

Fast and Slow Pain

A brief noxious stimulation of skin, such as pin prick or sudden exposure to extreme temperature, i.e. above 55°C, produces double pain, that is, fast and slow pain.

- **Fast pain:** Fast pain is due to stimulation of 'A' delta fibers. This causes bright, sharp and localization of pain.
- **Slow pain:** This is the second component of pain. It is due to the stimulation of 'C' nonmyelinated fibers. The pain is dull, intense, diffuse and unpleasant feeling.

Acute and Chronic Pain

Acute pain: Acute pain typically arises from soft tissue trauma or inflammation, e.g. postoperative surgical pain. Although it does not serve a protective function, acute pain does play a biologically adoptive role by facilitating tissue repair and healing. This is achieved by hypersensitizing the injured area and surrounding tissue to all types of stimuli such as contact with any external stimulus is avoided and repair process can continue undisturbed.

Chronic pain: Chronic pain persists beyond the expected time for a given disease process or injury, and has been arbitrarily defined as having a duration greater than 3–6 months. Such pain arises as a result of sustained, noxious input such as ongoing inflammation or it may be autonomous, with no temporal relation to the inciting cause. Chronic pain may manifest itself spontaneously, or it may be provoked by various external stimuli. The response is typically exaggerated in duration or amplitude or both. Examples of chronic pain are cancer pain, osteoarthritis pain, post-amputated phantom limb pain, etc. in all cases, chronic pain is maladapted and offers no useful biological function or survival advantage with the nervous system itself actually becoming the focus of the pathology. Therefore, chronic pain implies more than just duration, it is debilitating affliction that has a significant impact on patient's quality of life.

Psychological Pain

The perception of pain results from the brain's processing of new sensory input with existing memories and emotions, in the same way that other perceptions are produced. Childhood experiences, cultural attitudes, hereditary and gender are factors which contribute to the development of each individual's perception and response to different types of pain. Although some people may be able to withstand pain better than others, cultural factors rather than hereditary usually account for that ability. The point at which a stimulus begins to become painful is the 'pain perception threshold'. 'The pain tolerance threshold' is the point at which pain becomes unbearable, which varies significantly in certain groups. Social non-emotional response to an injury may be a sign of bravery in certain social and cultural groups. Depression and anxiety can lower both types of pain thresholds. Anger or excitement, however, can obscure or lessen pain temporarily. Feelings of emotional relief can also lessen a painful sensation.

MECHANISM OF PAIN

Pain originates from the pain receptors called 'nociceptors'.

Nociceptors

Nociceptors were discovered by Charles Scott Sherrington in 1906. Nociceptors are the specialized sensory receptors responsible for detection of noxious stimuli, transferring the stimuli into electrical stimuli then to electrical signals, which are then conducted to the central nervous system. These are the free nerve endings of primary afferent 'A' delta and 'C' fibers. These receptors are located in skin, viscera, muscles, joints, meninges, etc. They can be stimulated by mechanical, thermal and chemical stimuli. Whenever the tissue is damaged by trauma or by inflammation, certain chemical substances like bradykinins, serotonin, prostaglandins, cytokines and hydrogen ions are released and they stimulate nociceptors directly.

PAIN PATHWAYS

Pain pathway originates from nociceptors and carried through the afferent fibers to the center. Main afferent fibers which carry pain impulses are 'A' delta and 'C' fibers. In addition to these fibers, 'A' beta fibers carry noxious stimuli. 'A' beta fibers are highly myelinated and a large diameter that allow rapid conduction of signals. They have a low activation threshold and usually respond to light touch and transmit non-noxious stimuli.

'A' delta fibers are slightly myelinated and smaller diameter and conduct impulse more slowly than 'A' beta fibers. They respond to mechanical and thermal stimuli. They carry rapid, sharp and localized pain and responsible for initial reflex response to acute pain.

'C'fibers are unmyelinated and are the smallest type of primary afferent fibers. They conduct slow signals. These fibers are polymodel, respond to chemical, mechanical and thermal stimuli and carry slow, diffuse and dull pain.

Pain Pathway in the Spinal Cord

Primary afferent fibers enter the spinal cord through the dorsal column and synapse with the secondary afferent neurons in the dorsal horn of the spinal cord. Dorsal horn is divided histologically into 10 layers called 'Rexed laminas'. 'A' delta and 'C' fibers transmit information into Rexed lamina I and II, in addition to other laminas. Primary afferent terminals release a number of excitatory neurotransmitters which include glutamate and substance 'p'. Several complex interactions take place in the dorsal horn cells between afferent neurons, interneurons and descending modullary pathways. These interactions determine activity of the secondary afferent neurons. Glycine and GABA are important transmitters acting at inhibitory interneurons.

Ascending Tracts in the Spinal Cord

There are two main pathways which carry pain sensation to higher centers in the brain.

1. Spinothalamic tract
2. Spinoreticular tract

Spinothalamic Tract

As name indicates, this tract arises from the spinal cord and ends at thalamus. Second order of afferent neurons decussates within a few segments at the level of entry into the spinal cord and ascends in the contralateral spinothalamic tract to the nuclei in the thalamus. Third order of neurons then ascends to terminate into somatosensory cortex. There is also projection to the periaquiductal gray matter. The spinothalamic tract transmits signals that are important for localization of pain.

Spinoreticular Tract

These fibers also decussate and cross the opposite side of the cord and ascend to reach the reticular formation in the brain-stem. Then the fibers project into the thalamus and hypothalamus and further projection to the somatic area of the cortex. This pathway is involved in the emotional aspect of pain.

Pain Processing in the Brain

The somatosensory cortex is the important area for localization of pain. However, functional magnetic resonance imaging (MRI) has demonstrated that large area in the brain activated during the acute pain experience, often this area is called 'pain matrix'. The common areas which activated are primary and secondary somatosensory areas, insular, anterior cingulated gyrus, prefrontal cortex and the thalamus, demonstrating that these areas are all important in pain perception.

Inhibition of Pain Sensation

There are mechanisms which inhibit pain transmission at the spinal cord level through the descending pain inhibitory pathway from higher centers.

GATE CONTROL THEORY OF PAIN (Fig. 1.1)

Gate control theory of pain was proposed by Melzack and Wall in 1965 to describe a process of inhibitory pain modulation at the spinal cord level. It helps to explain why and when we bang our head; it feels better when we rub it. According to this theory, pain is determined by interaction of three systems in the dorsal column of the spinal cord. These systems are:

1. **T cells** (central transmission cells) in the dorsal column activate lateral spinothalamic tract (LSST).
2. **The afferent system** in the dorsal column acts as a central control trigger which regulates the gate control system. By activating 'A' delta fibers with tactile, non-noxious stimuli (touch fibres) stimulate both T cells and inhibitory cells in substatia gelatinosa in the dorsal column. Activation of small peripheral fibers, such as pain fibers, causes stimulation of T cells with inhibition of inhibitory neurons of substantia gelatinosa cells (SG cells).
3. **The inhibitory cells of gelatinosa** in the dorsal column regulate the afferent pattern before they influence the cells in the following way.

Activity in SG cells is increased by A alpha or beta cell fibers and decreased by small C fibers. SG cells inhibit activity in the afferent fiber terminals of both large and small fibers. Therefore, stimulation of T cells by large fibers is rapidly cut off by negative feedback through SG cells and conversely stimulation of T cells by small fibers will be increased by positive feedback through inhibition of SG cell activity.

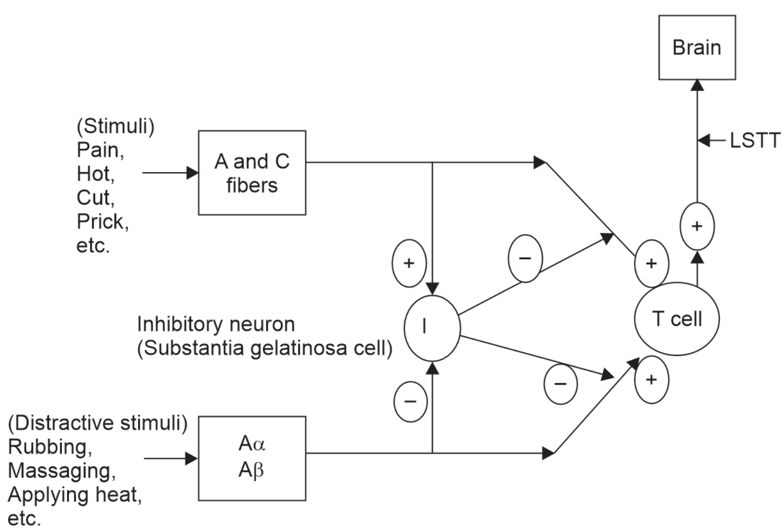

Fig. 1.1: Gate control theory of pain

Thus the dorsal horn acts as "gate" through which pain impulses reach the lateral spinothalamic tract. Stimulation of large fibers "closes the gate" whereas small fiber stimulation "opens the gate".

DESCENDING PATHWAY OF INHIBITION

The periaquiductal gray area in the midbrain and the rostral ventromedial medulla (nucleus raphe magnus), substantia nigra and basal ganglia contain high concentration of opioid receptors and endogenous opioids. From these areas, descending pathway projects to the dorsal horn cells of the spinal cord. When these areas are stimulated the inhibitory impulses reach the second order nociceptive dorsal horn cells and inhibit them causing anesthesia.