

211MDS

Pain theories

- **Definition**

In 1986, the International Association for the Study of Pain (IASP) defined pain as a sensory and emotional experience associated with real or potential injuries, or described in terms of such injuries. Painful manifestations can be explained on the basis of neural substrates mediating the sensory, affective, and nociceptive functions, as well as neuro-responses. While the sensory, discriminative–perceptive component permits the spatial and temporal localization, physical qualification and the intensity quantification of the noxious stimulus, the cognitive–affective component attributes emotional coloring to the experience, being responsible for the behavioral response to pain.

- **Peripheral receptors**

The propagation of pain is initiated with the activation of physiological receptors, called nociceptors, widely found in the skin, mucosa, membranes, deep fascias, connective tissues of visceral organs, ligaments and articular capsules, periosteum, muscles, tendons, and arterial vessels. The receptors correspond to free nerve endings and represent the more distal part of a first-order afferent neuron consisting of small-diameter fibers, with little or unmyelinated, of the A-Delta or C type, respectively. Their receptor fields can consist of areas ranging from small regions to regions measuring several millimeters in diameter, or even of more than one site in distant territories

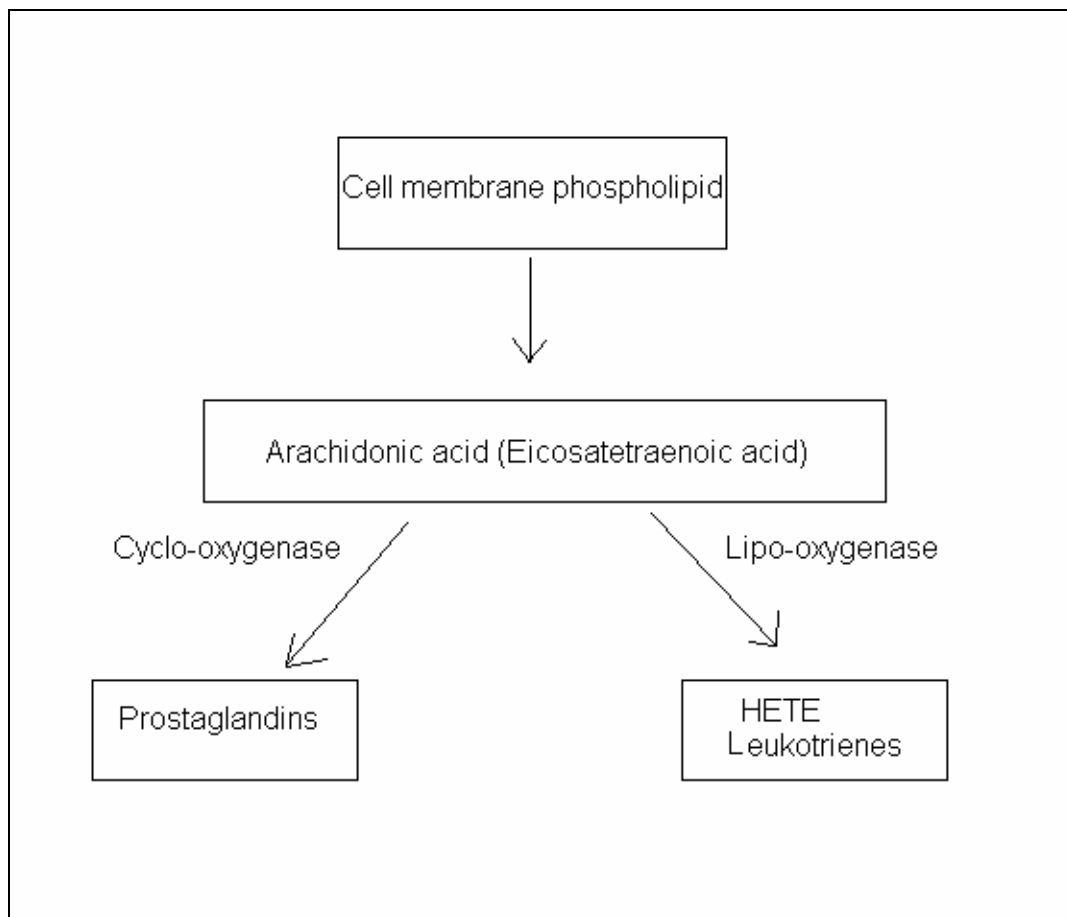
- **Pain Mediators:**

Many types of dental pain arise as a result of infection or damage to tissue. Both events initiate an inflammatory response that is intimately linked with pain. The passage of nociceptive impulses generated in the peripheral nerve fibers depends on

the release of various neurotransmitters. These neurotransmitters act either peripherally or centrally.

Examples of pain mediators include the following:

- Plasma kinins: e.g. bradykinin
- Serotonin
- Histamine
- Prostaglandins
- Leukotrienes
- Cytokines
- Neuropeptides



Pain is provoked when a variety of substances are released or injected into the tissues. These pain-producing substances can be released by trauma, infection, allergenic reaction, neurogenic reflexes and central changes from cell membranes, mast cells and nerve endings. This leads to the excitation of free nerve endings which act as nociceptors or peripheral sense organs that respond to noxious

stimulus. This group of substances include histamine, bradykinin, potassium, acetylcholine, prostaglandins, leukotrienes, and the neuropeptides. Arachidonic acid is derived from cell membrane phospholipids by the action of enzyme phospholipase A2. This enzyme is activated by trauma or infection. Once released, arachidonic acid is acted on by two further enzyme systems. Cyclo-oxygenase activity results in the formation of prostaglandins, thromboxane, and prostacycline, whereas lipo-oxygenase activity results in the production of the leukotrienes.

- **Nerve fibers:**

First-order afferent fibers are classified in terms of structure, diameter, and conduction velocity. C-type fibers are unmyelinated, ranging in diameter from 0.4 to 1.2 μm and have a velocity of 0.5–2.0 m/s; A-Delta fibers are barely myelinated, ranging in diameter from 2.0 to 6.0 μm and have a velocity of 12–30 m/s. The A-Beta fibers are myelinated, with a diameter of more than 10 μm and a velocity of 30–100 m/s, and do not propagate noxious potentials in normal situations; however, they are fundamental in the painful circuitry because they participate in the mechanisms of segmental suppression.

In the presence of a noxious stimulus, the primary nociceptive afferents show differentiated patterns of propagation. The A-Delta fibers propagate modally specific information, with marked intensity and short latency. They promote a quick sensation of first phase or acute pain, triggering withdrawal actions. The C-type fibers propagate information in a slower way, at times secondary to the action of the A-Delta afferents. Their prolonged potentials undergo summation along time and induce the manifestations of dull pain. Although widely used, this differentiation does not apply to all organs, being more evident in the skin.

- **Spinal cord:**

When approaching the spinal cord, large nerve fibers detach from thicker fibers, organizing themselves in the ventrolateral bundle of roots. They form synapses with second-order neurons distributed along the dorsal horn of the spinal cord. About one-

third of the ventral roots are sensitive and predominantly painful, although their cell bodies are located in the dorsal root ganglion. The integration with the neurons of the dorsal horn of the spinal cord occurs after the passage through the anterior horn or by the fibers that, before penetrating in the ipsilateral anterior horn, are directed to the dorsal horn.

Pain Control Theories

Specificity theory:

Specific stimulus has a specific receptor which goes to a location in the brain. The specific location identifies the pain's quality. Thus any noxious stimulus applied to the surface of the skin results in a pain sensation. The evaluation of the type of pain occurs in the brain.

Pattern Theory:

A pattern or coding of sensory information is created by different sensations. This theory is faulty due to the number of different types of receptors proven to exist.

Sensory Interaction Theory:

It is based on that the intensity of the stimulus and central summation were the critical determinants of pain. This theory proposes that pain is not a separate entity but results from over-stimulation of other primary sensations (touch, light, sound, etc.).

Gate Control Theory

- It was proposed by Melzack & Wall in 1965
- Substantia Gelatinosa (SG) in dorsal horn of spinal cord acts as a 'gate' – only allows one type of impulses to connect with the 2nd order neuron

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Action potential

The neuron:

It is the nerve cell which is able to transmit messages between the nervous system and all parts of the body. Neuron is composed of three main parts: the dendrites or nerve endings, the axon and the cell body. Nerve cells that conduct impulses from the central nervous system toward the periphery are termed motor neurons while the ones which transmit impulses from the periphery to the higher centers are called sensory neurons.

The axon:

It is a long extension of the neural cytoplasm encased in a thin sheath called the nerve membrane of the axolemma.

- ✦ Afferent (Ascending) – transmit impulses from the periphery to the brain
 - First Order neuron
 - Second Order neuron
 - Third Order neuron
- ✦ Efferent (Descending) – transmit impulses from the brain to the periphery

First Order Neurons

- ✦ Stimulated by sensory receptors
- ✦ End in the dorsal horn of the spinal cord
- ✦ Types of nerve fibers
 - A-alpha – non-pain impulses
 - ✦ Large, myelinated
 - ✦ Low threshold mechanoreceptor; respond to light touch & low-intensity mechanical info
 - A-delta – pain impulses due to mechanical pressure
 - ✦ Large diameter, thinly myelinated

- ✦ Short duration, sharp, fast, bright, localized sensation (prickling, stinging, burning)
- ✦ C – pain impulses due to chemicals or mechanical
 - ✦ Small diameter, unmyelinated
 - ✦ Delayed onset, diffuse sensation (aching, throbbing)

Second Order Neurons

- ✦ Receive impulses from the first order neuron in the dorsal horn
 - ✦ Lamina II, Substantia Gelatinosa (SG) - determines the input sent to T cells from peripheral nerve
 - ✦ Travel along the spinothalamic tract
 - ✦ Pass through Reticular Formation
 - ✦ Ends in thalamus

Third Order Neurons

- ✦ Begins in thalamus
- ✦ Ends in specific brain centers (cerebral cortex)
 - ✦ Perceive location, quality, intensity
 - ✦ Allows to feel pain, integrate past experiences & emotions and determine reaction to stimulus

Neurotransmitters

- ✦ They are chemical substances that allow nerve impulses to move from one neuron to another
- ✦ Found in synapses
- ✦ Examples include:
 - ✦ Substance P - thought to be responsible for the transmission of pain-producing impulses
 - ✦ Acetylcholine – responsible for transmitting motor nerve impulses
 - ✦ Enkephalins – reduces pain perception by bonding to pain receptor sites

- ✳ Can be either excitatory or inhibitory

Resting membrane potential:

- Resting membrane Potential: a chemical and electrical balance with a pump to aid in return to homeostasis.
 - The resting membrane potential for a neuron is approximately -70mV
 - At rest it is permeable to sodium ions
 - Freely permeable to potassium ions
 - Freely permeable to chloride ions
 - At rest the ions are distributed as in the following table:

| Ion | Intracellular (mEq/L) | Extracellular (mEq/L) |
|-----------|-----------------------|-----------------------|
| Potassium | 110-170 | 3-5 |
| Sodium | 5-10 | 140 |
| Chloride | 5-10 | 110 |

Depolarization:

Excitation of a nerve segment leads to rapid influx of sodium into the nerve cell which causes depolarization of the nerve from its resting state to a firing threshold of approximately -50 to -60 mV. When the firing threshold is reached a massive increase in the influx of sodium occurs. At the end of depolarization (peak of the action potential), the electrical potential of the nerve is actually reversed. The entire depolarization process takes around 0.3 ms.

Repolarization:

Repolarization is caused by inactivation of membrane permeability to sodium to return the nerve cell to its resting stage. In order to move sodium against its concentration gradients the sodium potassium pump plays an important role in the repolarization step.

Threshold

The minimum amount of stimulus necessary to create an action potential

Refractory periods

- Refractory period: membrane potential goes below the resting potential of -70mV and may not be stimulated for a given period of time. This limits how many action potentials may be produced
 - Absolute refractory period: NO stimulus will create a response no matter how strong
 - Relative refractory period: resting potential is much lower, therefore a higher stimulus is needed

Theories of local anesthetic action:

- 1- Acetylcholine theory
- 2- Calcium displacement theory
- 3- Surface charge theory
- 4- Membrane expansion theory
- 5- Specific receptor theory

The most favored theory is the specific receptor theory. It proposes that local anesthetic acts by binding to specific receptors on the sodium channel. The action of the local anesthetic is direct and not mediated by some changes in the general properties of the cell membrane.