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Pain: A review

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Abstract
According to the international association for the study of pain, pain is "an unpleasant sensory and emotional experience associated with actual and potential tissue damage, or described in terms of such damage, or both. Thus pain has objective, physiologic sensory aspects as well as subjective emotional and psychological components. The term "Nociception" is used only to describe the neural response to traumatic or noxious stimuli. Pain is often mistreated or undertreated and can lead to depression, insomnia, lethargy and reduced physical and mental functioning. The successful drug management of pain relies on selecting the appropriate drug at the correct dosage and balancing efficacy against adverse effects.
The present paper reviews the Introduction, types, physiology, mechanism, pathways and its management.

Keywords: Pain, Nociceptive, Neuropathic, Analgesic.

Introduction
Pain is a common symptom and is important because it both signals 'disease' and aids diagnosis. Irrespective of cause, its relief is one of the most important duties of a doctor. Fortunately, pain relief was one of the earliest triumphs of pharmacology, although clinicians have only recently started to use the therapeutic armamentarium that is now available adequately and rationally [1].

Pain is a Protective Mechanism
Pain occurs whenever any tissue are being damaged, and it cause the individual to react to remove the pain stimuli. Even such simple activities as sitting for a long time on the Ischia can cause tissue destruction because of lack of blood flow to the skin where it is compressed by weight of the body. When the skin become painful as a result of the ischemia, the person normally shifts weight subconsciously. But a person who has lost the pain sense, as after spinal cord injury, fails to feel the pain and, therefore, fails to shift. This soon results in total breakdown and desquamation of the skin at the areas of pressure [11].

Pain Receptors and their Stimulation
Pain Receptors are Free Nerve Endings
The pain receptors in the skin and other tissues are all free nerve endings. They are widespread in the superficial layer of the *skin* as well as in certain internal tissues, such as the *periosteum*, the *arterial walls*, the *joint surfaces*, and the *falx* and *tentorium* in the cranial vault. Most other deep tissues are only sparsely supplied with pain endings; nevertheless, any widespread tissue damage can summate to cause the slow chronic acting type of pain in most of these areas.

Type of stimuli pain receptors
There are three type of stimuli pain receptors.
1. Mechanical
2. Thermal
3. Chemical

Pain can be elicited by multiple type of stimuli. In general, fast pain is elicited by the mechanical and thermal type of stimuli, whereas slow pain can be elicited by all three types. Some of the chemicals that excite the chemical type of pain are *bradykinin, serotonin, histamine, potassium ions, acids, acetylcholine,* and *proteolytic enzymes*. In addition, *prostaglandins* and *substance* P enhance the sensitivity of pain endings but do not directly excite them. The chemical substance are especially important in stimulating the slow, suffering type of pain that occurs after tissue injury.

Non- adapting Nature of Pain Receptors
In contrast to most other sensory receptors of the body, pain receptors adapt very little and sometimes not at all. In fact, under some conditions, excitation of pain fibers becomes progressively greater, especially so for slow-aching-nauseous pain, as the pain stimulus continuous. This increase in sensitivity of the pain receptors is called hyperalgesia. One can readily understand the importance of this failure of pain receptors to adapt, because it allows the pain to keep the person apprised of a tissue damaging stimulus as long as it persist.

Types of Pain
There are two type of pain
1. Fast
2. Slow

Fast Pain
The perception of Fast pain occurs very rapidly, usually within 0.1 second after a stimulus is applied, because the nerve impulses propagate along medium diameter, myelinated a fibers. This type of pain is also known as acute, sharp, or pricking pain. The pain felt from a needle puncture or knife cut to the skin is fast pain. Fast pain is not felt in deeper tissue of the body.

Slow Pain
The perception of slow pain by contrast, begins a second or more after a stimulus is applied. It then gradually increases in intensity over a period of several seconds or minutes. Impulses

for slow pain conduct along small diameter, unmyelinated C fibers. This type of pain, which may excruciating, is also referred to as chronic, burning, aching, or throbbing pain. Slow pain can occur both in the skin and in deeper tissues or internal organs. An example is the pain associated with a toothache [12].

Types of Pain Basis of the Presumed Pathophysiology

On the basis of pathophysiology the pain is divided into three category-

1. Somatic

Fracture
Incisional injury
Thermal injury
Traumatic injury

2. Visceral

Bowel obstruction
Constipation
Endometriosis
Metastatic organ involvement

3. Deafferentation

Alcoholic and nutritional neuropathy
Diabetic mono neuropathy and polyneuropathy
Pancoast's tumor
Postherpetic neuralgia [2]

1. Pain is a silent epidemic in the United States. An estimated 50 million Americans live with chronic pain caused by disease, disorder or accident. An additional 25 million people suffer acute pain resulting from surgery or accident [3].
2. Approximately two third of these individual in pain have been living with this pain from more than five years [4].
3. The most common type of pain include arthritis, lower back, bone/joint pain, muscle pain and fibromyalgia [3].
4. The loss of productivity and daily activity due to pain is substantial. In a study done in 2000 it was reported that 36 million Americans missed work in previous year due to the pain and that 83 million indicated that pain affected their participation in various activities [5].
5. In 1986 Koch [6] estimated that 70 million office visit to physicians were motivated by pain complaints. In 1994, Joranson & Lietman [7] estimated that approx. one-fifth of the adult Americans population experienced chronic pain, and in 1999 Market data Enterprises [8] estimated that approx. 4.9 million individual saw a physician for chronic pain treatment.
6. In 1998 the National Institute of Health [9] estimated that approx. 80% of nursing home residents suffering pain were under treated.
7. A survey done by the American pain Society [4] in 1999 revealed that more than four out of ten people suffering moderate to severe pain were unable to find adequate pain relief.

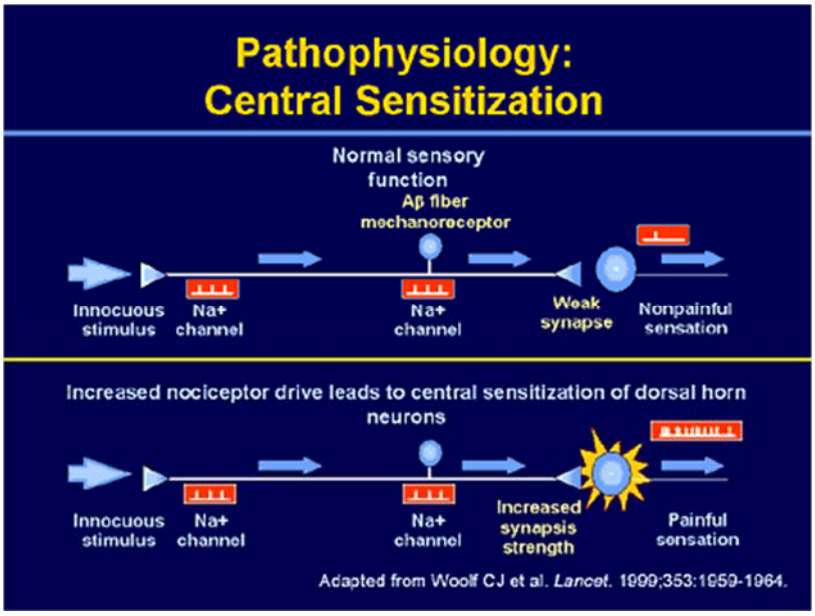
Physiology of Pain

There are two major mechanism in the physiology of pain:

1. **Nociceptive (sensory):** Inflammatory pain due to chemical, mechanical, and thermal stimuli at the nociceptors.
2. **Neuropathic:** pain due to neural damage in peripheral nerves or within the central nervous system. During normal physiology, pain sensation are elicited by activity in unmyelinated (C-) and thinly myelinated primary afferent neurons that synapse with neurons are the dorsal horn of the spinal cord. Sensory information is then relayed to the thalamus and brainstem. Repetitive activation of C- nociceptive receptors produces alterations in central as well as peripheral nervous systems.

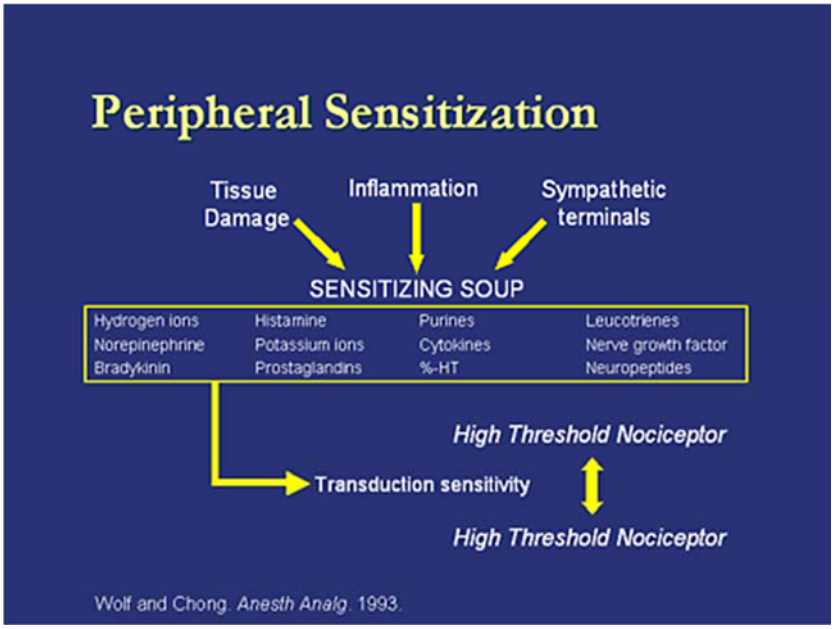
The Mechanism of Central Sensitization [31]

The response in the CNS are primarily physiological, central sensitization is a physiological process and, only if there is continual firing of C-nociceptors over time, will these process leads to more chronic pain syndromes. Sustained or repetitive C-nociceptor activity produces alterations in the response of the central nervous system to inputs from the periphery. When identical noxious stimuli are repeatedly applied to skin at a certain rate, there is a progressive build-up in the response of spinal cord dorsal horn neurons. This process, called central sensitization, occurs with any tissue damage.



The Mechanism of Peripheral Pain Sensitization [32]

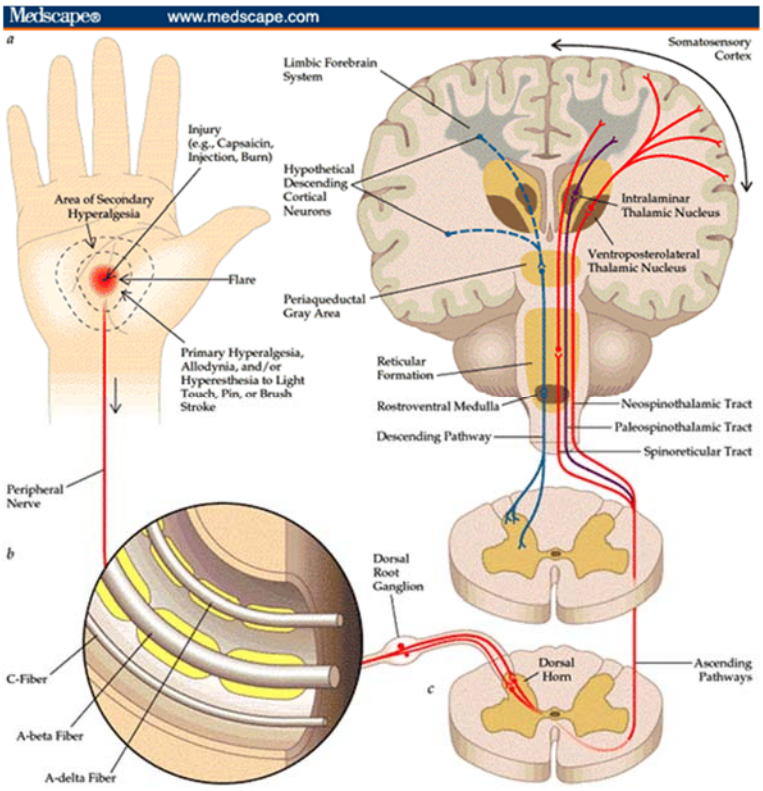
Normally, C-fibers are silent in the absence of stimulation, but following acute tissue injury in presence of ongoing pathophysiology, these nociceptors become sensitized and release a complex mix of pain and inflammatory mediators leading to pain sensations [10].



Neuroanatomy of Pain Pathways [33]

Sensory receptors for pain, nociceptors, are naked nerve endings that terminate in the skin and most other tissues of the body. However, their distribution is not uniform throughout organs of the body. As a general rule, deep visceral organs of the body are not well supplied with nociceptors. These receptors are generally classified according to the type to which they respond:

1. Mechanosensitive pain receptors respond to mechanical damage.
2. Thermosensitive pain receptors respond to temperature extremes.
3. Chemo sensitive pain receptors respond to chemicals that occur with damaged tissues, example hypertonic saline, potassium chloride, acetylcholine, 5-Hydroxytryptamine, histamine, bradykinin and substance P. Vasoactive amines are released just after injury by the basophiles, platelets and mast cells.

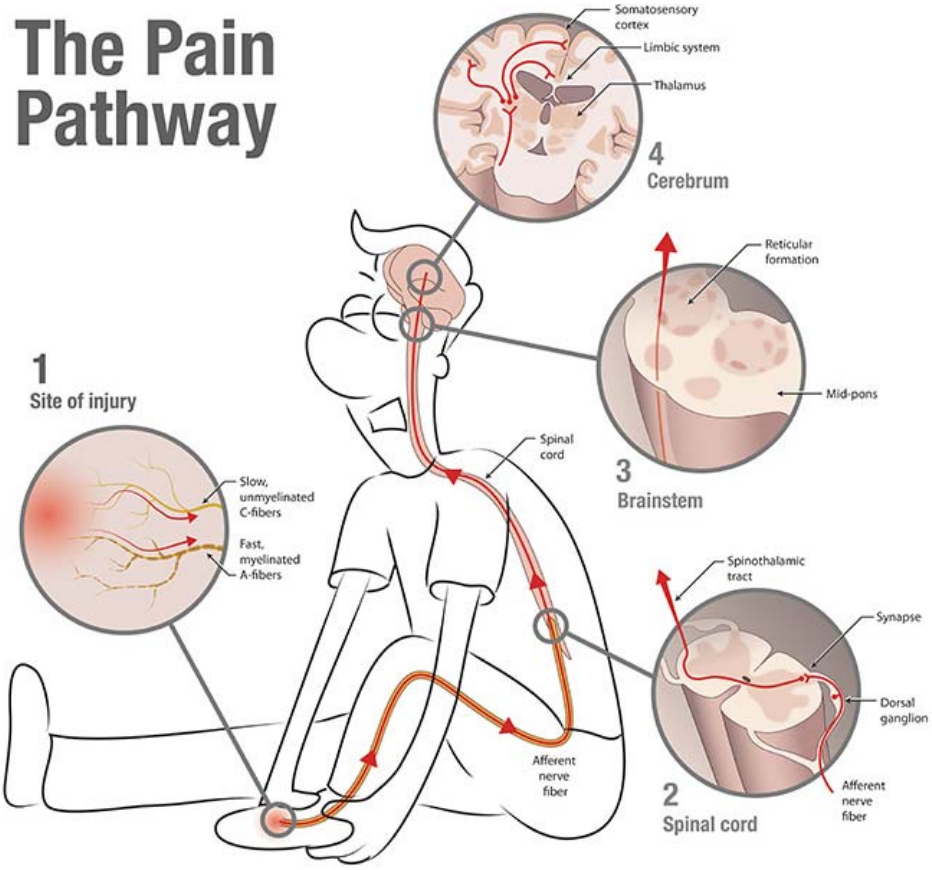


Dual Pathways for the Transmission of Pain Signals into the Central Nervous System

Even through all pain receptors are free nerve endings, these endings use two separate pathways for transmitting pain signals into the central nervous system. The two pathways mainly correspond to two type of pain – *a fast sharp pain pathway* and *a slow chronic pain pathway*.

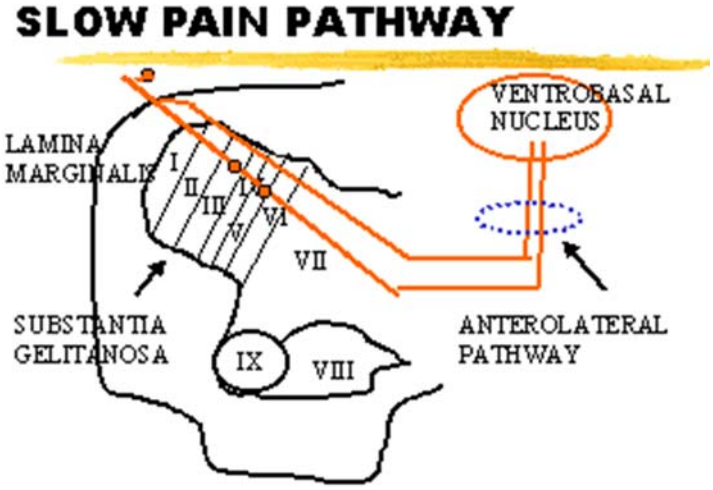
Peripheral Pain Fibers –"Fast" and "Slow" Fibers [34]

The sharp pain signals are elicited by either mechanical or thermal pain stimuli; they are transmitted in the peripheral nerves to the spinal cord by small type A delta fibers at velocity between 6 and 30m/sec. conversely, the slow chronic type of pain is elicited mostly by chemical types of pain stimuli but sometimes by persisting mechanical or thermal stimuli. This slow chronic pain is transmitted to the spinal cord by type C fibers at velocities between 0.5 and 2m/sec.

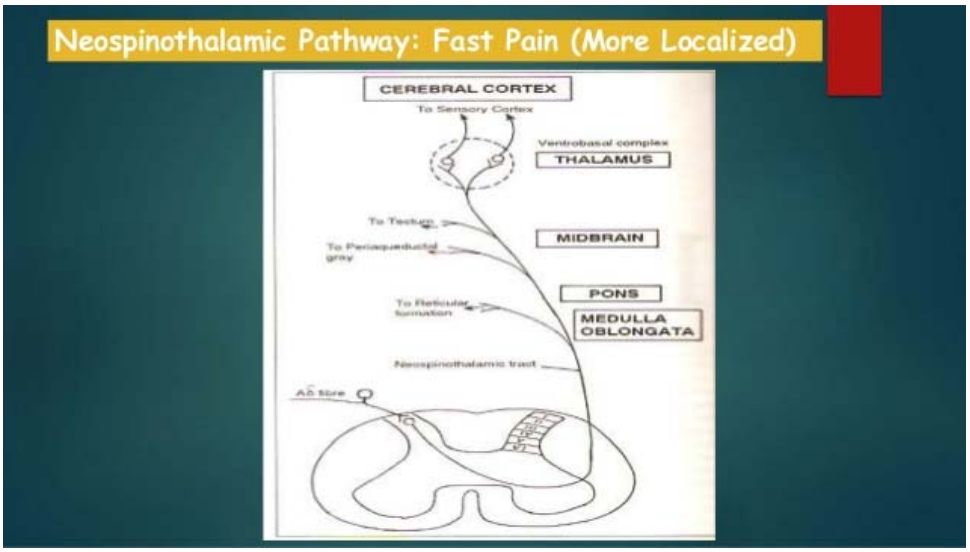


The Pain Pathway

Because of this double system of pain innervations, a sudden painful stimulus often given a "double" pain sensation: a fast sharp pain that is transmitted to the brain by the A delta fiber pathway, followed a second or so later by a slow pain that is transmitted by the C fiber pathway. The sharp pain apprises the person rapidly of a damaging influence and, therefore, plays an important role in making the person react immediately to remove himself or herself from the stimulus [35].



The slow pain tends to the become greater over time. The slow pain tends to become greater over time. This sensation eventually produces the intolerable suffering of long continued pain and makes the person keep trying to relieve the cause of the pain. On entering the spinal cord from the dorsal spinal roots, the pain fibers terminate on relay neurons in the dorsal horns. Here again, there are two system processing the pain signals on their way to the brain [13],



Fibers and enhanced pain sensitivity, in part a consequence of increased excitability of central neurons in the spinal cord [36].

Natural Molecules Responsible For Pain

Bradykinin, released from plasma kininogen, and cytokines, such as TNF-a, IL-1, IL-8, appear to be particularly important in eliciting the pain of inflammation. These agents liberate prostaglandins and probably other mediators that promote hyperalgesia. Neuropeptides, such as substance P and calcitonin gene related peptide also may be involved in eliciting pain.

The capacity of prostaglandins to sensitize pain receptors to mechanical and chemical stimulation apparently from a lowering of the threshold of the polymodal nociceptors of C fibers. In general, NSAIDs do not affect hyperalgesia or pain caused by the direct action of prostaglandins, consistent with the notion that the analgesic effect of these agents are due to inhibition of prostaglandins synthesis [14].

Management of Pain [19, 20, 21]

The treatment of the pain require the main three methods:

Medication [22, 23, 24]

Acute pain is usually managed with medications such as analgesics and anesthetics. Management of chronic pain, however, is much more difficult and may require the coordinated efforts of a pain management team, which typically includes medical practitioners, clinical psychologists, physiotherapists, occupational therapists, physician assistants, and nurse practitioners.

Physiological [25, 26, 27]

Individuals with more social support experience less cancer pain, take less pain medication, report less labor pain and are less likely to use epidural anesthesia during childbirth or suffer from chest pain after coronary artery bypass surgery.

Alternative Medicine [28, 29, 30]

Pain is the most common reason for people to use complementary and alternative medicine. meta-analysis of randomized clinical trials found that spinal manipulation was "more effective than sham therapy but was no more or less effective than general practitioner care, analgesics, physical therapy, exercise, or back school" in the treatment of low back pain.

Defination of Analgesic

Analgesic are those agents that decrease pain without loss of consciousness are referred to as analgesic, or analgetics. Although analgesic is grammatically correct, common use has made analgesic preferable to analgetic for the description of the pain killing drug. Pain relieving agents are also called anti-nociceptive.

Mechanism of Pain and Actions of Analgesic Drugs

1. Nociceptive and pain involve peripheral and central mechanism; ‘gating’ mechanism in the spinal cord and thalamus are key features.
2. Pain differs from nociceptive because of central mechanism, including an emotional component.
3. Many mediators are implicated, including prostaglandins, various peptides that act on micro receptors like 5HT, noradrenaline and anandamide.
4. Analgesic inhibit, mimic or potentiate neutral mediators like aspirin inhibits prostaglandins biosynthesis.

Sites of Action of Analgesic

- Drug can prevent pain:
- At the site of injury (e.g., NSAIDs);
- By blocking peripheral nerves (local anesthetics);
- By closing the 'gates' in the dorsal and thalamus;
- By altering the central appreciation of pain [15].

Conclusion

Pain is a feeling triggered in the nervous system. Pain may be sharp or dull. It may come and go, or it may be constant. You may feel pain in one area of your body, such as your back, abdomen, chest or you may feel pain all over, such as when your muscles ache from the flu. Pain can be helpful in diagnosing a problem. Without pain, you might seriously hurt yourself without knowing it, or you might not realize you have a medical problem that needs treatment. Once you take care of the problem, pain usually goes away. However, sometimes pain goes on for weeks, months or even years. Pain is the most common reason for people to use complementary and alternative medicine. Acute pain is usually managed with medications such as analgesics and anesthetics. Management of chronic pain, however, is much more difficult and may require the coordinated efforts of a pain management team, which typically includes medical practitioners, clinical psychologists, physiotherapists, occupational therapists, physician assistants, and nurse practitioners.

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