

Pain

(Pathophysiology & Management)

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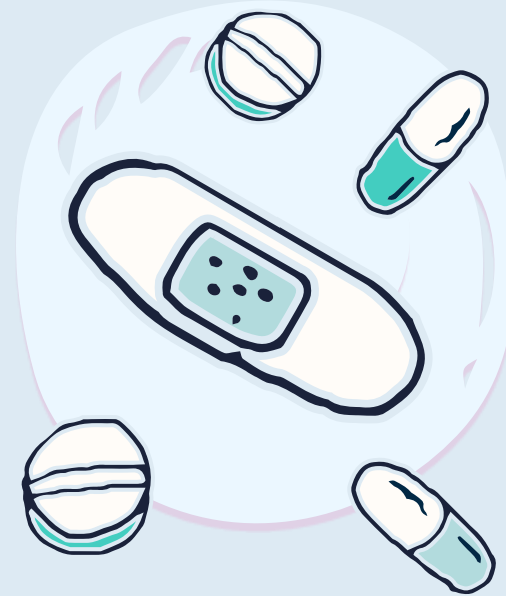
Considerations before recommending a pain regimen



What is Pain?

"A subjective experience with two complementary aspects:

- **Localized sensation in a particular body part**
- **Unpleasant quality of varying severity commonly associated with behaviors directed at relieving the experience"**

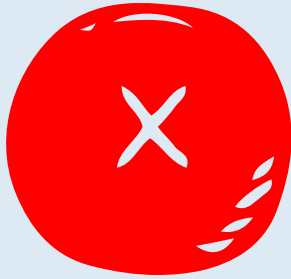


What is normal pain processing?

1. **Transduction**: Processes by which tissue-damaging stimuli activate nerve endings.
2. **Transmission**: Relay functions by which the message is carried from the site of tissue injury to the brain regions underlying perception.
3. **Modulation**: Neural process by which the body alters a pain signal as it is transmitted along the pain pathway
4. **Perception**: Subjective awareness produced by sensory signals.



Accompanying Pathologies



Inflammation



Collective response of chemical mediator and cellular defenses to an injury or infection.



Fever



System-wide sign of inflammation that raises the body temperature and stimulates an immune response.



Types of Pain



Nociceptive Pain

Caused by stimuli that threaten or result from bodily tissue damage.

Somatic: From skin, bone, joint, muscle or connective tissue → **Aching, stabbing, throbbing, pressure**
Visceral: From internal organs → **Gnawing, cramping, aching, sharp**



Neuropathic Pain (Sharp, Tingling, Burning, Shooting)

Results from maladaptive response to damage or disease of somatosensory nervous system.



Nociplastic Pain

Accompanies both nociceptive and neuropathic pain.



Mechanisms of Pain Types



Nociceptive Pain

Activation of nociceptors sensitive to noxious stimuli.



Neuropathic Pain

Lesions of the nervous system from peripheral nociceptor to the brain.



Nociplastic Pain

Not fully understood.

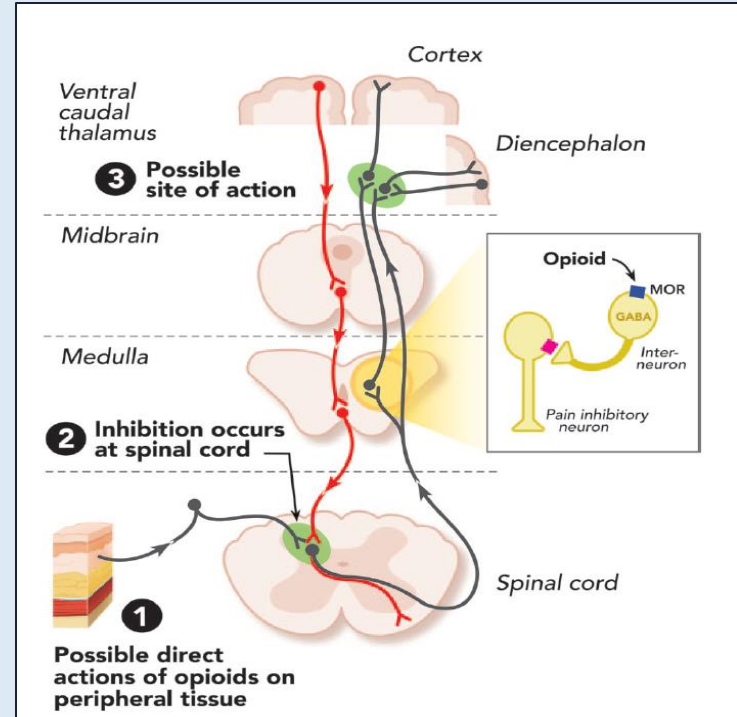


Overview of Pain Pathways

Primary neuron: site of pain to spinal cord

Secondary neuron: spinal cord to thalamus

Tertiary Neuron: thalamus to several areas of the brain



Primary Neuron



A- β Fibers

Respond to stimuli that stimulate opioid neurons to release endogenous opioids.



A- δ and C Fibers

Bring the pain signal to the spinal cord.

Releases pain mediators such as **glutamate, CGRP and substance P** to the spinal cord synapse.



Secondary Neuron



Cognitive Pathway (FAST)

Project to the thalamus and somatosensory cortex*

***ALLOWS** person to identify type and location of pain



Affective Pathway (SLOW)

Project to the thalamus and to:

NRM, PAG: Triggers the descending inhibitory pathway

ACC: Triggers sensitive and affective memory

PAG = Periaqueductal gray nucleus
NRM = Nucleus Raphe Magnus
ACC = Anterior Cingular Cortex



Tertiary Neuron

(Descending Pathway)



PAG

Stimulates descending pathway which releases 5-HT into the dorsal horn of the spinal cord.

5-HT = Serotonin



NRM

Stimulates descending pathway which releases NE into the dorsal horn of the spinal cord.

NE = Norepinephrine

PAG = Periaqueductal gray nucleus
NRM = Nucleus Raphe Magnus



Drug Targets for Pain

1.

Neuroreceptors

Opioids, Tramadol

2.

Ion Channels

Lidocaine, Gabapentin

3.

Neurotransmitters

Amitriptyline, Duloxetine
and Clonidine



What should be considered before recommending a pain regimen?

Past medical history

Surgical history

Social and Family
History

Psychiatric
comorbidities



What should be considered before recommending a pain regimen?



Location of Pain

Pain history

Pain Characteristics

Pain severity and impact



OLDCARTS pain history

▪ O nset ("When did your pain start?")
▪ L ocation ("Where does it hurt?")
▪ D uration ("How long does your pain last?")
▪ C haracter ("How does your pain feel?", ie, aching, burning, shooting, tingling)
▪ A lleviating/ A ggravating ("What makes your pain better/pain worse?") and A ttribution ("What do you think is the cause?")
▪ R adiation ("Does this pain spread anywhere else?")
▪ T emporal pattern ("Does your pain vary over the course of a day?")
▪ S ymptoms associated ("How does your pain impact your physical function, your mood, your sleep?")

The questions represented by the acronym "OLDCARTS" can be used to broadly characterize pain. For patients who report multiple sites of pain, the questions should be asked for each site.

References

1. Institute of Medicine (US) Committee on Pain, Disability, and Chronic Illness Behavior. Pain and Disability: Clinical, Behavioral, and Public Policy Perspectives. Washington (DC): National Academies Press (US); 1987. 7, The Anatomy and Physiology of Pain. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK219252/> Accessed at August 9, 2023.
2. Physiopedia. Pain Modulation. Available from: <https://www.physio-pedia.com/Pain-Modulation>. Accessed at August 9, 2023.
3. Parker N, Schneegurt M, Hue Thi Tu A, et al. *Cascade Microbiology*. 1st ed. Mavs Open Press; 2019. Available at: https://batch.libretexts.org/print/url=https://bio.libretexts.org/Courses/Portland_Community_College/Cascade_Microbiology/11%3A_Innate_Nonspecific_Host_Defenses/11.5%3A_Inflammation_and_Fever.pdf. Accessed at August 9, 2023.
4. Tauben D, Stacey BR. Evaluation of chronic non-cancer pain in adults. In: Fishman, S, ed. UpToDate; 2023. Available at: https://www.uptodate.com/contents/evaluation-of-chronic-non-cancer-pain-in-adults?search=types%20of%20pain&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H2501150571. Accessed at August 9, 2023.
5. Scholz J. Mechanisms of chronic pain. *Mol Pain*. 2014;10(Suppl 1):O15. Published 2014 Dec 15. doi:10.1186/1744-8069-10-S1-O15
6. Finnerup NB, Kuner R, Jensen TS. Neuropathic Pain: From Mechanisms to Treatment. *Physiol Rev*. 2021;101(1):259-301. doi:10.1152/physrev.00045.2019
7. In: DiPiro JT, Yee GC, Posey L, Haines ST, Nolin TD, Ellingrod V. eds. *Pharmacotherapy: A Pathophysiologic Approach, 11e*. McGraw Hill; 2020. Accessed August 15, 2023. <https://accesspharmacy-mhmedical-com.proxy-ln.researchport.umd.edu/content.aspx?bookid=2577§ionid=248126979>
8. Obeng S, Hiranita T, León F, McMahon LR, McCurdy CR. Novel Approaches, Drug Candidates, and Targets in Pain Drug Discovery [published correction appears in *J Med Chem*. 2021 Aug 12;64(15):11746]. *J Med Chem*. 2021;64(10):6523-6548. doi:10.1021/acs.jmedchem.1c00028

Questions?

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