PAIN MANAGEMENT
ARE OPIOIDS THE BEST OPTION?

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DISCLAIMER

Vicky Shah declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings and honoraria

LEARNING OBJECTIVES – PHARMACISTS

Identify the types and classifications of pain

Describe the pain assessment process

Compare pharmacologic and nonpharmacologic pain management options

LEARNING OBJECTIVES – TECHNICIANS

Identify the types and classifications of pain

Describe the pain assessment process

Compare pharmacologic and nonpharmacologic pain management options

PRE-TEST QUESTION 1

True or False: All pain is treated exactly the same.

A. True

B. False

PRE-TEST QUESTION 2

Which of the following can be used as non-pharmacological treatment options for pain?

A. BRAT

B. RICE

C. DOLER

D. CURB

PRE-TEST QUESTION 3

Which of the following should be recommended for patients who are prescribed high doses of opioids? SELECT ALL THAT APPLY

A. Loperamide

B. Senna

C. Naloxone

D. Buprenorphine

IF WE KNOW THAT PAIN AND SUFFERING CAN BE ALLEVIATED, AND DO NOTHING ABOUT IT, THEN WE OURSELVES, BECOME THE TORMENTORS.

— PRIMO LEVI

Bennett DS, Breakthrough pain: Treatment rationale with opioids. Available at: http://www.medscape.org/viewarticle/461612.

WHAT IS YOUR DEFINITION OF PAIN?

WHAT IS PAIN?

"An unpleasant sensory and emotional response associated with actual or potential tissue damage or described in terms of such damage."

However, as pain is subjective, many clinicians define pain as "whatever the patient says it is."

Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. (September 2020). "The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises". *Pain*. 161 (9): 1976–1982. doi:10.1097/j.pain.0000000000001939. PMC 7680716. PMID 32694387.

NEW PAIN DEFINITION

"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage"

Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors

Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons

Through their life experiences, individuals learn the concept of pain

A person's report of an experience as pain should be respected

Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being

Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain

Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. (September 2020). "The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises". *Pain*. 161 (9): 1976–1982. doi:10.1097/j.pain.0000000000001939. PMC 7680716. PMID 32694387.

SIGNIFICANT MEDICAL PROBLEM

Nearly 50 million Americans report chronic pain

- 25% of all Americans experience pain lasting greater than 24 hours in the past month
  - 42% of these individuals have had pain lasting greater than one year

Annual cost is greater than $70 billion

Degradation of physical and emotional functions

Decreased quality of life

Loss of productivity/loss of work when not managed appropriately

Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2018;67(36):1001–1006. 10.15585/mmwr.mm6736a2

SIGNIFICANT MEDICAL PROBLEM

>126 million US adults (55.7%) experienced pain in the past 3 months

>50% of ED visits

Up to 80% report postoperative pain; up to 10% transition to chronic pain

39% reported back pain

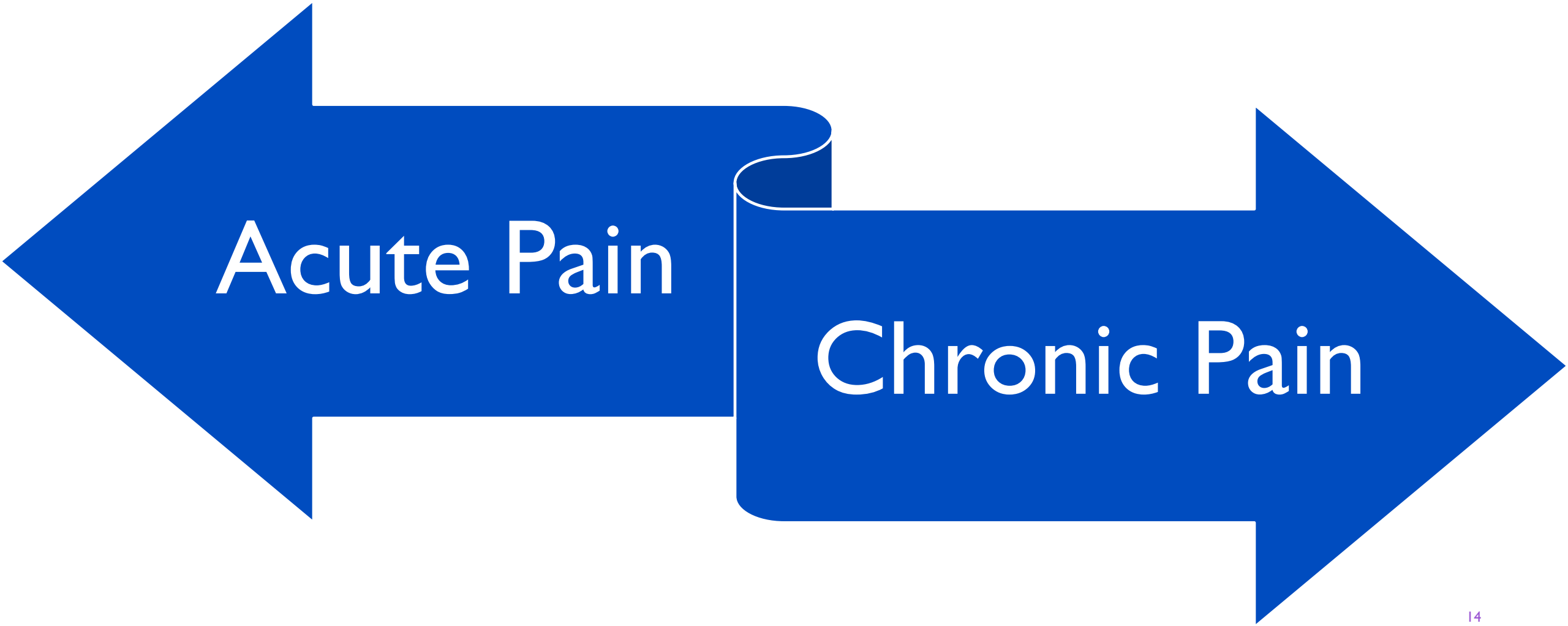
36.5% lower limb pain

30.7% upper limb pain

in the past 3 months

Up to 16% report pain due to headaches

Cordell W, et al. Am J Emerg Med 2002. 20(3):165-169; Glare P, et al. Lancet. 2019. 393(10180):1537-1546; Lucas JW, et al. CDC, NCHS Data Brief. 2021 Jul;(415):1-8; CDC, MMWR Morb Mortal Wkly Rep 2020;69:359.
Gomes T, Tadrous M, Mamdani M, et al. The burden of opioid-related mortality in the United States. *JAMA Network Open*. 2018;1(2):e180217.
Cicero TJ, Ellis MS, Kasper ZA. Increased use of heroin as an initiating opioid of abuse. *Addict Behav*. 2017;74:63-66.


Acute Pain
Chronic Pain

Characteristics	Acute Pain	Chronic Pain
Time	< 3 months Sudden/rapid onset	> 3 months Pain lasting past expected duration of healing
Examples	Broken bones, childbirth, burns, dental procedures, headaches, etc.	Malignancy, arthritis, fibromyalgia, neuropathic pain, AIDS, Multiple Sclerosis etc.
Dependence to Medications	Unusual	Common
Physiological Component	Not present	Present
Cause of Pain Known	Common	Possibly
Treatment Goal	Cure	Improve Functionality

Chou R et al. J Pain. 2016;17(2):131-157; Cohen SP et al. BMJ. 2008;337:a2718; Olesen J, Lipton RB. Curr Opin Neurol. 2004;17(3):275-282; Paice JA, Ferrell B. CA Cancer J Clin. 2011;61(3):157-182
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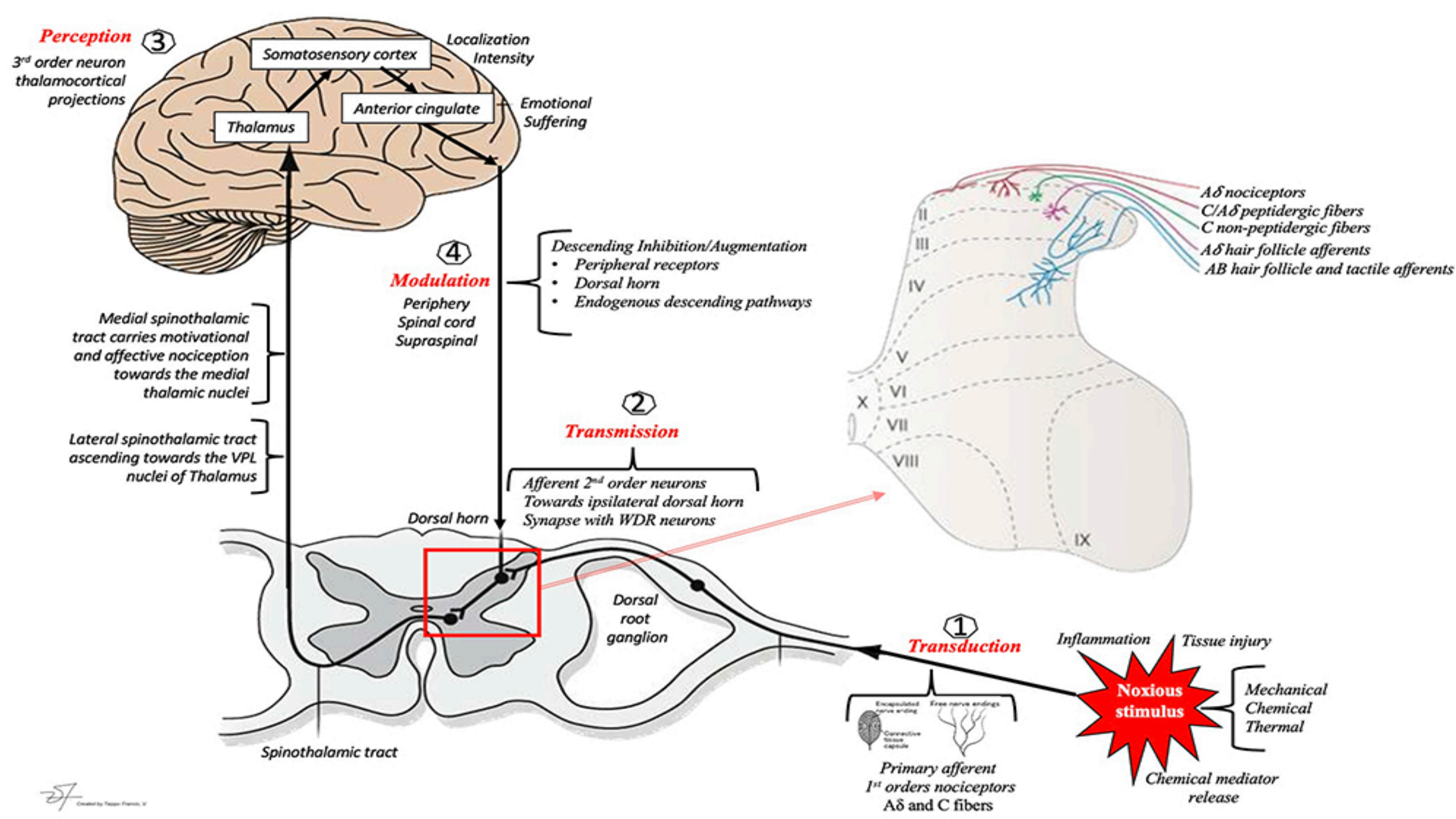
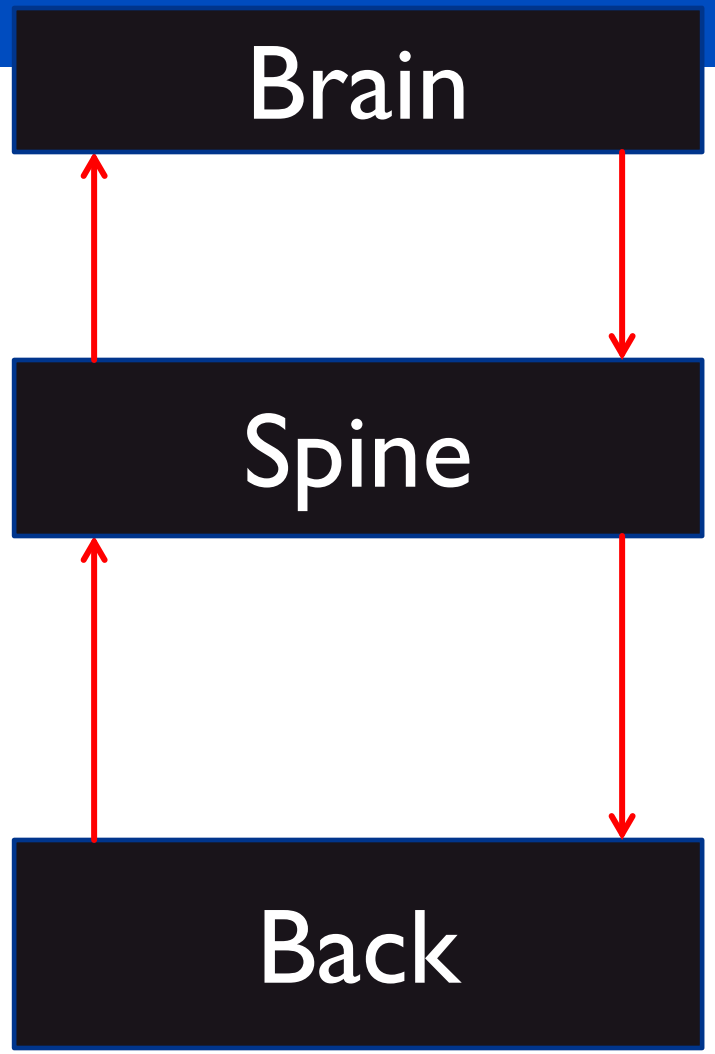
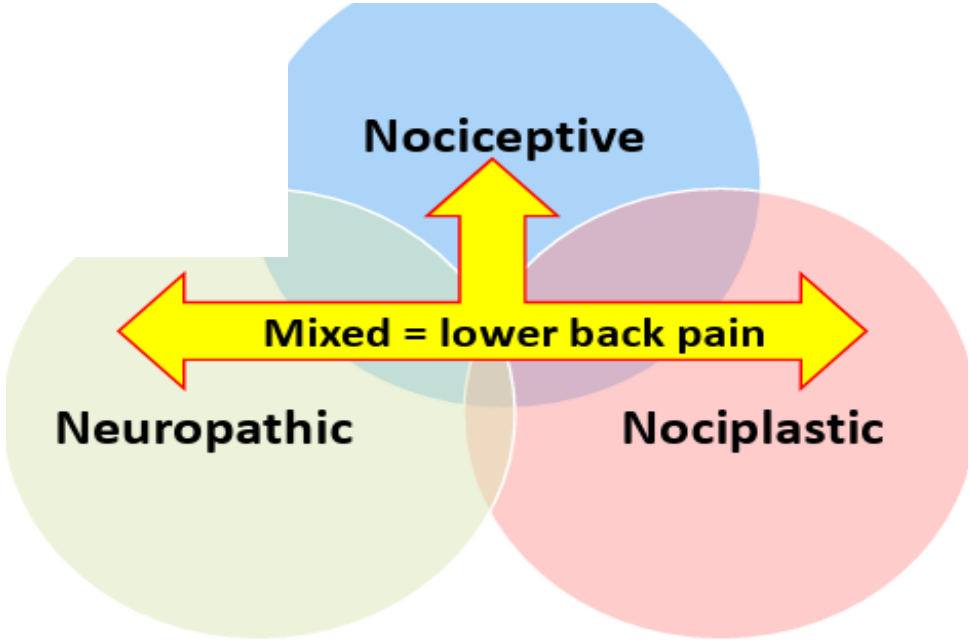
Powell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain – United States, 2016. *JAMA*. 2016.315(15):1624-1645.


Perception
3
3rd order neuron thalamocortical projections
Somatosensory cortex
Localization
Intensity
Thalamus
Anterior cingulate
Emotional
Suffering
4
Modulation
Periphery
Spinal cord
Supraspinal
Descending Inhibition/Augmentation
• Peripheral receptors
• Dorsal horn
• Endogenous descending pathways
Medial spinothalamic tract carries motivational and affective nociception towards the medial thalamic nuclei
Lateral spinothalamic tract ascending towards the VPL nuclei of Thalamus
2
Transmission
Afferent 2nd order neurons
Towards ipsilateral dorsal horn
Synapse with WDR neurons
Dorsal horn
Dorsal root ganglion
Spinothalamic tract
Aδ nociceptors
C/Aδ peptidergic fibers
C non-peptidergic fibers
Aδ hair follicle afferents
AB hair follicle and tactile afferents
II
III
IV
V
VI
VII
VIII
IX
X
1
Transduction
Primary afferent
1st orders nociceptors
Aδ and C fibers
Inflammation
Tissue injury
Noxious stimulus
Mechanical
Chemical
Thermal
Chemical mediator release

PAIN PATHWAY



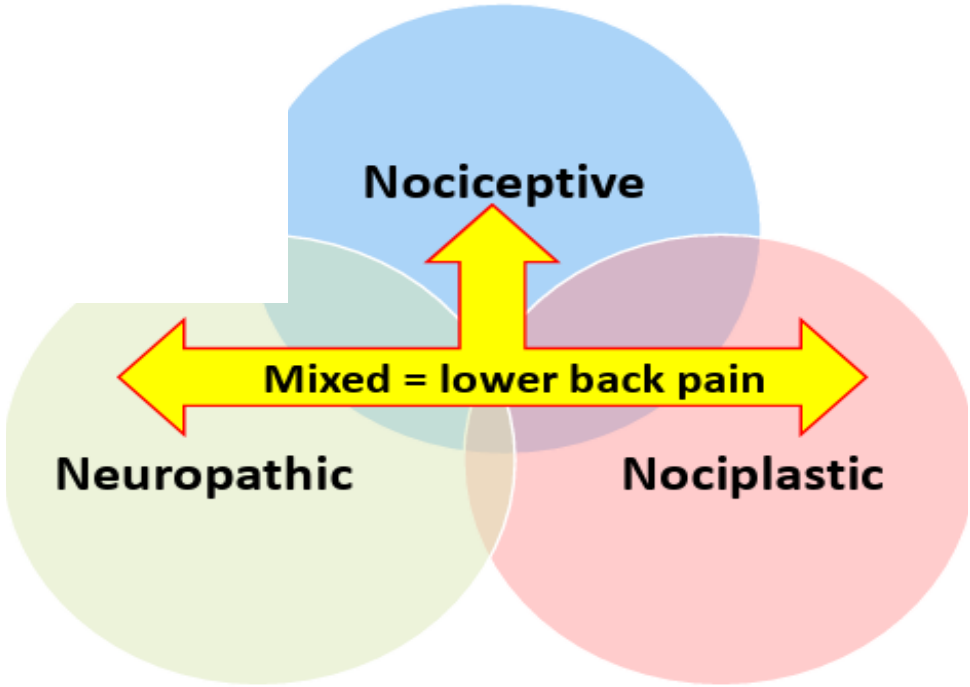
TYPES OF PAIN



Shraim MA, et al. Clin J Pain. 2020 Oct;36(10):793-812.

TYPES OF PAIN

Nociceptive pain
Damage to somatic or visceral tissue due to inflammation or trauma



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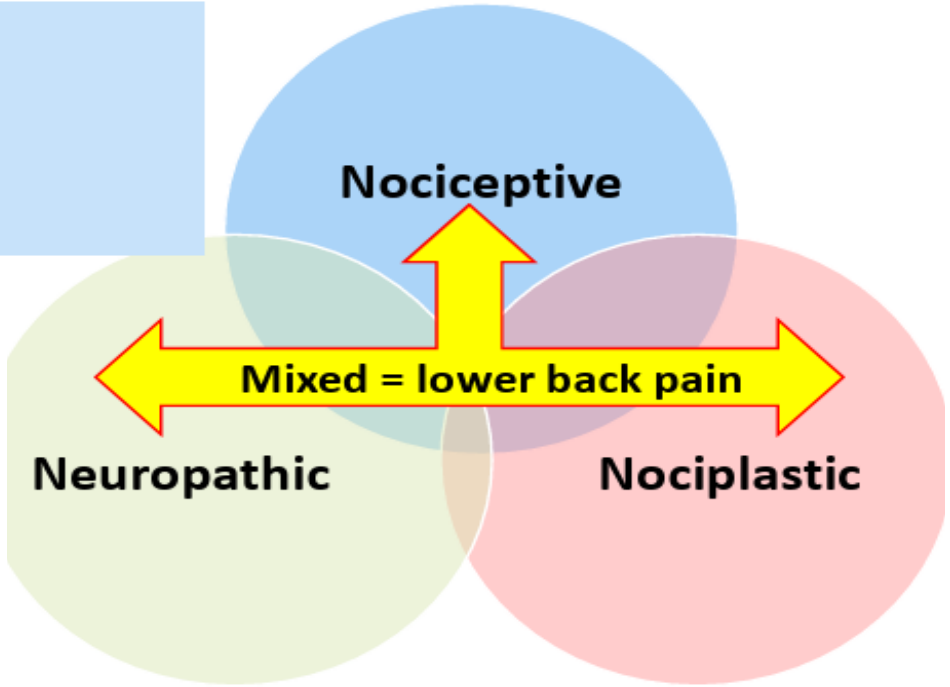
Damage to somatic or visceral tissue due to inflammation or trauma

Examples
- Bone fracture
- Infection
- Arthritis-related
- Appendicitis



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TYPES OF PAIN

Neuropathic pain
Peripheral or central nerve damage

Nociceptive pain
Damage to somatic or visceral tissue due to inflammation or trauma

Examples
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- Infection
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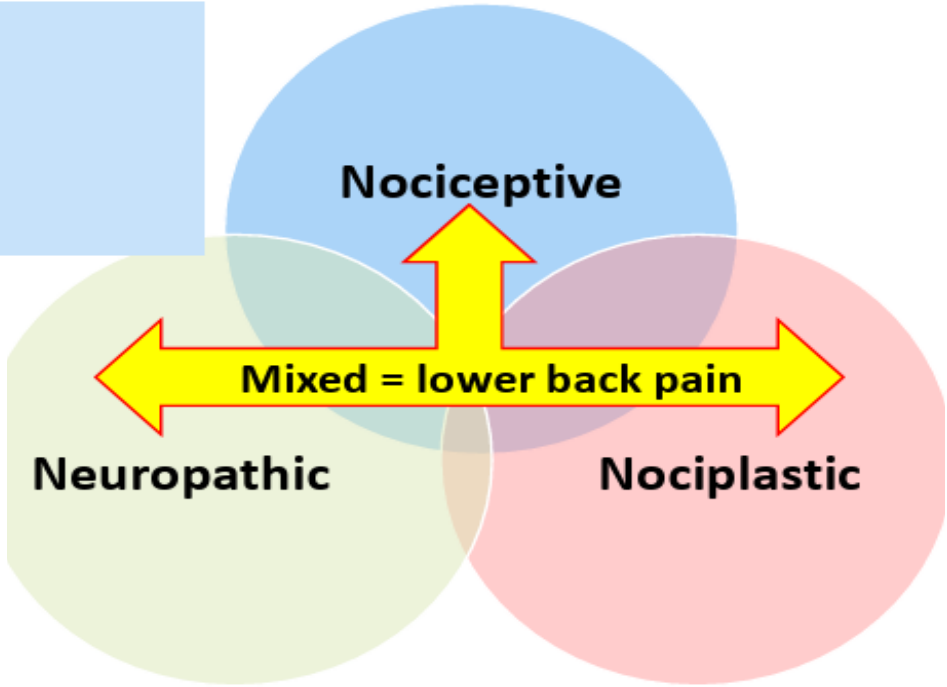

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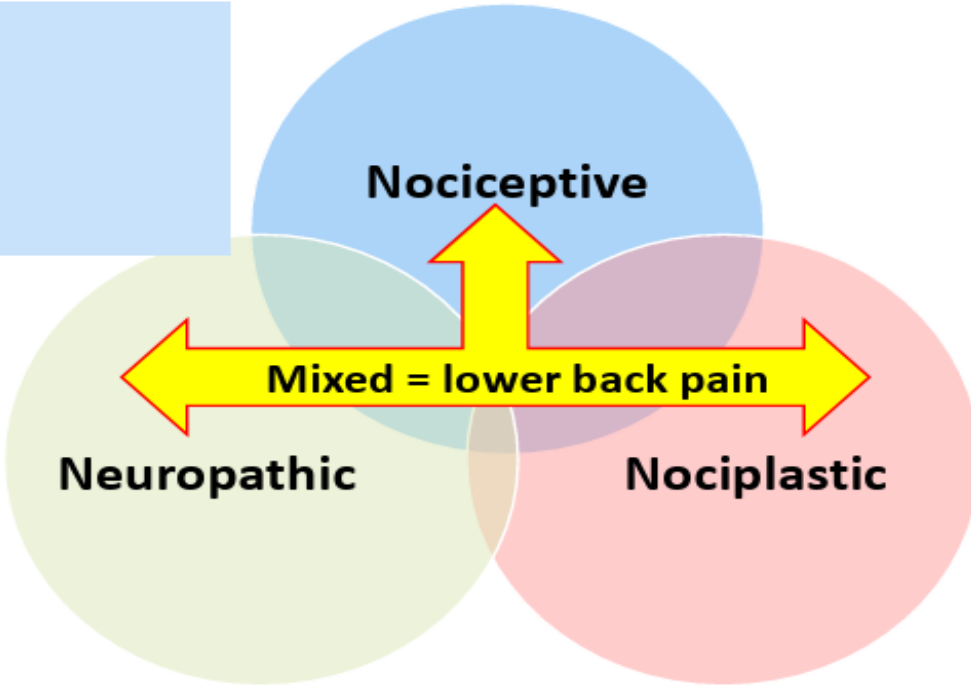

Examples
- Postherpetic neuralgia
- Diabetic neuropathy
- Sciatica

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TYPES OF PAIN

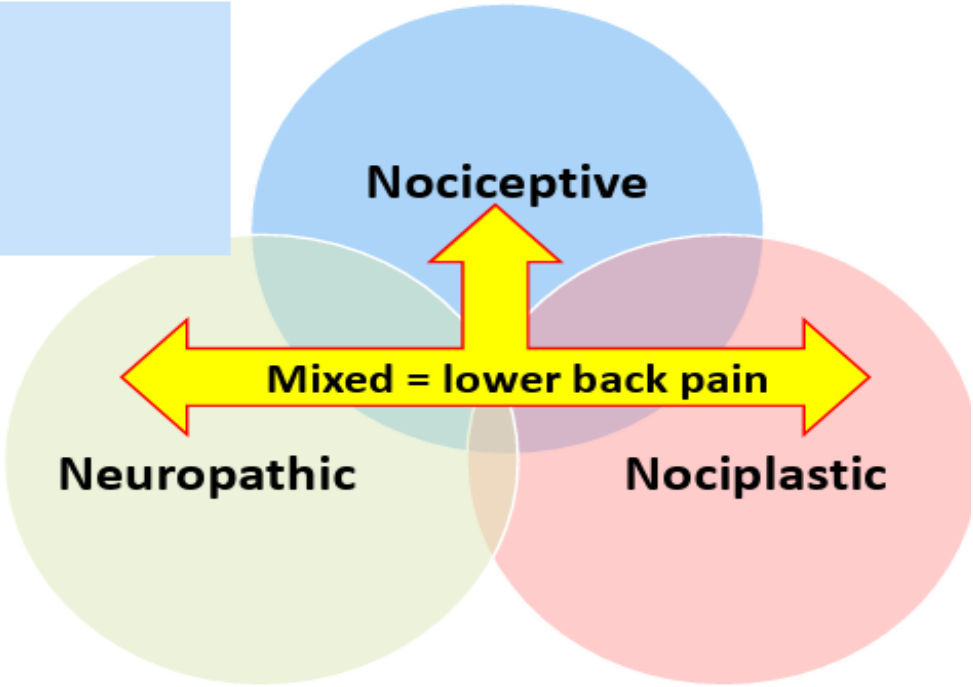
Neuropathic pain
Peripheral or central nerve damage

Nociceptive pain
Damage to somatic or visceral tissue due to inflammation or trauma

Nociplastic Pain
Void of identifiable nerve or tissue damage.

Potentially due to persistent neuronal dysregulation

Examples
- Bone fracture
- Infection
- Arthritis-related
- Appendicitis



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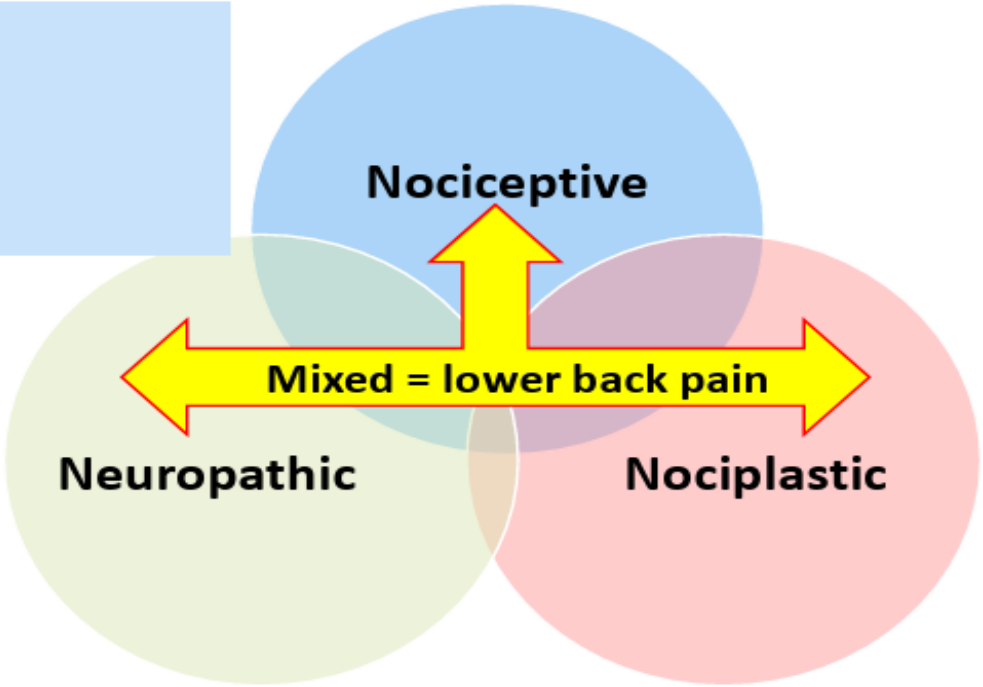

Examples
- Postherpetic neuralgia
- Diabetic neuropathy
- Sciatica

Examples
- Fibromyalgia
- Chronic lower back pain
- Inflammatory bowel disease

Shraim MA, et al. Clin J Pain. 2020 Oct;36(10):793-812.

TYPES OF PAIN

Nociceptive Pain

Somatic & Visceral Pain

- Described as sore, aching, dull, twisting, throbbing pain
- Scrapes, injuries, cramps
- Responds well to NSAIDs, APAP, Opioids and Muscle Relaxants

Neuropathic Pain

- Described as burning, electric, pins/needles, numbing pain
- Nerve damage or abnormal operations of the nervous system
- Responds best to anti-depressants or anticonvulsants

Shraim MA, et al. Clin J Pain. 2020 Oct;36(10):793-812.

PAIN SYMPTOMS

Distress	Change in appetite	Anxiety/Agitation	Fatigue	Depression	Anger/Fear
Hypertension	Tachycardia	Tachypnea	Pupil dilation	Pale skin	Sweating
Insomnia	Decreased physical activity	Loss of identity	Socially withdrawn/ isolation	Financial instability/loss of employment	

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EXPECTATIONS OF THE PATIENT

Purpose of therapy is to improve functionality to be able to complete normal daily activities

- Establish a function/quality of life goal and work towards this
  - Be able to sleep
  - Be able to take care of their kids
  - Small baby step goals are better than major long-term goals

Purpose of therapy is not to get pain to zero!

- Goal is to reduce pain by 30%

Patient must be an active/responsible partner on the team

Patient must be willing to listen to ALL recommendations including non-pharmacologic recommendations

NEVER PROMISE THE PATIENT THE PAIN WILL BE GONE

- Always be honest and upfront
- Medications work differently for each patient

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PAIN ASSESSMENT

Patient-oriented approach is the best option!

- Take a comprehensive history and physical examination
  - Pain is SUBJECTIVE NOT OBJECTIVE

Make all attempts to identify source of pain

Characterize the pain (acute vs. chronic, nociceptive vs. neuropathic)

Chou R et al. J Pain. 2016;17(2):131-157; Cohen SP et al. BMJ. 2008;337:a2718; Olesen J, Lipton RB. Curr Opin Neurol. 2004;17(3):275-282; Paice JA, Ferrell B. CA Cancer J Clin. 2011;61(3):157-182
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PQRSTU MNEMONIC

Palliating/Precipitating Factors	• What makes your pain better? Worse? Movement? Hygiene care?
Quality	• Describe your pain for me
Radiation	• Does the pain move from one place to another or does it stay in one place? Where?
Severity/Site of Pain/Sleep	• On a scale of 0-10 with 0 = no pain and 10 = worst pain possible, where is you pain now? At its worst? At its best? After you take pain medication? How are you sleeping with the pain?
Temporal Nature/Time of Day	• Is you pain constant or intermittent? How long have you had this pain?
YOU	• What are your pain management goals including intensity, quality of life and activity level? What does your pain mean to you?

Chou R et al. J Pain. 2016;17(2):131-157; Cohen SP et al. BMJ. 2008;337:a2718; Olesen J, Lipton RB. Curr Opin Neurol. 2004;17(3):275-282; Paice JA, Ferrell B. CA Cancer J Clin. 2011;61(3):157-182
Coda BA, Bonica JJ (2000). "General considerations of acute pain". In Panswick CC, Main CJ (eds.). *Pain management: an interdisciplinary approach*. Edinburgh: Churchill Livingstone. ISBN 978-0443056833.

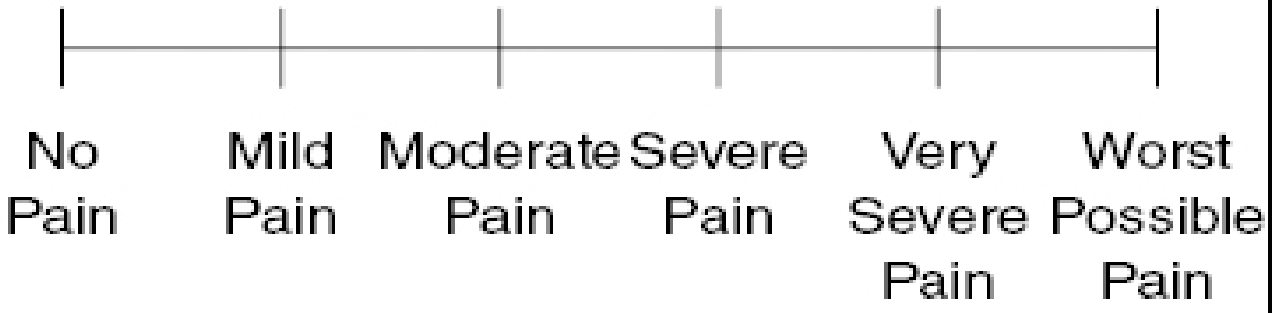
OLD CARTS

Onset	• When did the pain start, or how long has it been going on?
Localized	• Where is the pain?
Description	• Explain how the pain feels: burning, aching, sharp, stabbing, throbbing
Characteristics	• Describe how the pain feels (i.e., aching, burning)?
Alleviating/Aggravating	• Is there anything that makes the pain better or worse?
Radiation	• Does the pain spread anywhere else?
Time	• How long have you had the pain and has it been constant or intermittent?
Symptoms:	• Has the pain had an impact on any other of your daily activities, such as eating, sleeping, or mood?

University of California. UCSD's Practical Guide to Clinical Medicine. UCSD. San Diego. 2018. https://meded.ucsd.edu/clinicalmed/history.htm.

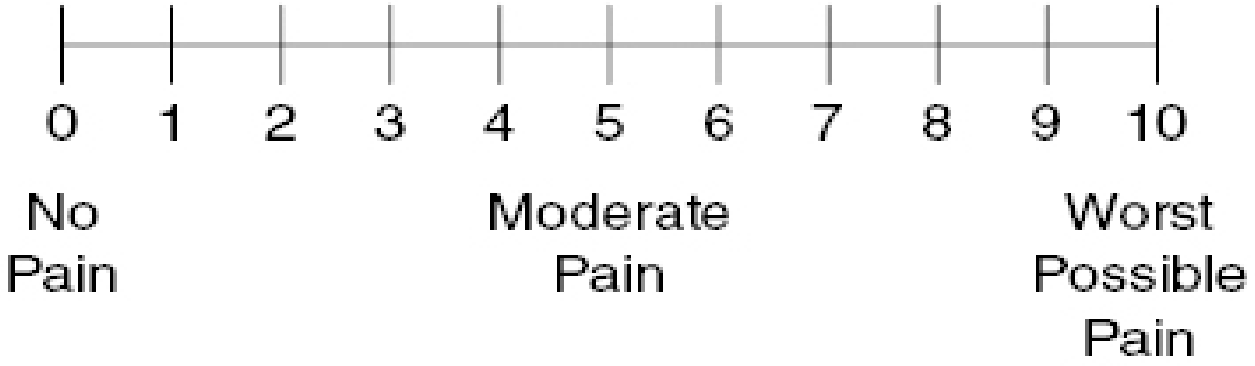
PAIN SCALES

Verbal Pain Intensity Scale



Visual Analogue Scale

0–10 Numeric Pain Intensity Scale



Wong-Baker FACES® Pain Rating Scale

WHAT TOOLS CAN WE UTILIZE IN THE INTENSIVE CARE UNIT IF THE PATIENT CANNOT DIRECTLY TELL US THEIR PAIN SCALE?

Critical Pain Observational tool (CPOT)	Score	Behavioral Pain scale (BPS)	Score
Facial expressions:		**Facial expressions:**	
• *Relaxed, Neutral*	0	• *Relaxed*	1
• *Tense*	1	• *Partially tightened*	2
• *Grimacing*	2	• *Fully tightened*	3
Body movements		**Upper limbs**	
• *Absence of movements or normal position*	0	• *No movement*	1
• *Protection*	1	• *Partially bent*	2
• *Restlessness /agitation*	2	• *Fully bent with finger flexion*	3
		• *Permanently retracted*	4
Compliance with the ventilator (intubated patients)		**Compliance with ventilation**	
• *Tolerating ventilator or movement*	0	• *Tolerating movement*	1
• *Coughing but tolerating*	1	• *Coughing but tolerating ventilation for most of the time*	2
• *Fighting ventilator*	2	• *Fighting ventilator*	3
		• *Unable to control ventilation*	4
Vocalization (non-intubated patients)			
• *Talking in normal tone or no sound*	0		
• *Sighing, moaning*	1		
• *Crying out, sobbing*	2		
Muscle tension			
• *Relaxed*	0		
• *Tense, rigid*	1		
• *Very tense or rigid*	2		

BPS >5, or CPOT >3 are indicative of significant pain

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TREATMENTS

TREATMENT PLANS

Provide treatment plan based on patient's description of their level of pain

Provide non-pharmacologic and pharmacological treatment options

Ask proper questions to help determine appropriate therapy

Do not assume that all patient's are drug seeking

Chou R et al. J Pain. 2016;17(2):131-157; Cohen SP et al. BMJ. 2008;337:a2718; Olesen J, Lipton RB. Curr Opin Neurol. 2004;17(3):275-282; Paice JA, Ferrell B. CA Cancer J Clin. 2011;61(3):157-182
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NON-PHARMACOLOGICAL THERAPIES

- Physical Manipulation
- Heat/Cold Application
- Massage
- Acupuncture
- Exercise
- Transcutaneous Electrical Nerve Stimulation
- Relaxation Training
- Imagery
- Hypnosis
- Cognitive Behavior Therapy

Myers, S, Vigar, V. The State of the Evidence for Whole-System, MultiModality Naturopathic Medicine: A Systematic Scoping Review. J Altern Complement Med. 2019; 25(2):141–168.
Islam S, Frey N. Psychotherapy for the Treatment of Acute Musculoskeletal Pain: A Review of Clinical Effectiveness and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2020 Apr 17. PMID: 33074632.

HOW DOES MASSAGE THERAPY HELP WITH PAIN?

HOW DOES THERMAL THERAPY HELP WITH PAIN?

Chandler A, Preece J, Lister S. Using heat therapy for pain management (clinical practice). Nursing Standard. 2002;17(9):40+.

WHAT IS RICE THERAPY?

SHOULD ALL PATIENTS WITH PAIN BE STARTED ON OPIOIDS?

PHARMACOLOGICAL THERAPIES

- Non-Opioids
- Opioids
- Anti-Depressants
- Anti-Convulsants
- Muscle Relaxants

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WHO TREATMENT LADDER

Step 1 Mild Pain

Nonopioid analgesics:
- Acetaminophen
- Aspirin
- NSAIDs

Step 2 Moderate Pain

Moderate Opioids:
- Tramadol
- Codeine
- Hydrocodone
- Oxycodone

+ nonopioid adjuvants

Step 3 Severe Pain

Strong Opioids:
- Morphine
- Levorphanol
- Meperidine
- Hydromorphone
- Oxycodone
- Fentanyl

Anekar AA, Hendrix JM, Cascella M. WHO Analgesic Ladder. [Updated 2023 Apr 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554435/
Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016 [published correction appears in MMWR Recomm Rep. 2016;65(11):295]. MMWR Recomm Rep. 2016;65(1):1-49. Published 2016 Mar 18. doi:10.15585/mmwr.rr6501e1. Erratum in. MMWR Recomm Rep. 2016;65(11):295

NON-OPIOID ANALGESICS

- Acetaminophen (APAP)
- Aspirin (ASA)
- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Considered first-line agents for the treatment of mild-moderate pain

Do not produce tolerance, psychological, or physical dependence

Ceiling effects after long periods of time

Unless contraindicated, should be included in all pain regimens as adjunctive therapies

Anekar AA, Hendrix JM, Cascella M. WHO Analgesic Ladder. [Updated 2023 Apr 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554435/
Moor RA, Wiffen PJ, Derry S, et al. Non-prescription (OTC) oral analgesics for acute pain – an overview of Cochrane reviews. *Cochrane Database Syst Rev*. 2015;11:CD010794.

ACETAMINOPHEN

Functions in the central nervous system and is effective in reducing mild to moderate pain and reducing fever

Does not have anti-inflammatory effects compared to NSAIDs

Lower gastrointestinal bleeding risk compared to NSAIDs

Major concern for hepatotoxicity especially in higher doses

- Maximum daily dose of 4000mg per day
- Recommended to avoid doses greater than 3000mg per day
- Lower recommended dose of 2000-3000mg for older patients with hepatic impairment

Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Nonopioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. Br J Anaesth. 2017 Jan;118(1):22-31. doi: 10.1093/bja/aew391. PMID: 2803923
Yoon E, Babar A, Choudhary M, Kutner M, Pyrsopoulos N. Acetaminophen-Induced Hepatotoxicity: a Comprehensive Update. J 39 RxCe.com Clin Transl Hepatol. 2016;4(2):131-142. doi:10.14218/JCTH.2015.00052

NSAIDS

Work by inhibiting cyclooxygenase enzymes, COX-1 and COX-2 and are effective for mild to moderate pain relief, reduce inflammation and help control high fever

- COX-1 is responsible for production of prostaglandins involved in physiological functions, such as renal homeostasis and platelet aggregation
- COX-2 is found in inflammatory cells and produces prostaglandins involved in inflammation, pain, and fever
- Nonselective NSAIDs (such as diclofenac and ibuprofen) inhibit COX-1 and COX-2, whereas selective inhibitors (celecoxib) block COX-2

Adverse Effects

- Gastrointestinal bleeding
- Gastrointestinal effects including irritation, nausea and abdominal pain
- Issues with hypertension and renal dysfunction

Topical NSAIDs such as diclofenac are effective for osteoarthritis and have limited systemic side effects

Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Nonopioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. Br J Anaesth. 2017 Jan;118(1):22-31. doi: 10.1093/bja/aew391. PMID: 28039239

WHAT QUESTIONS SHOULD YOU ASK BEFORE DETERMINING WHICH NON-OPIOID TO INITIATE?

OPIOIDS

Adams JFA. Substitutes for Opium in Chronic Diseases. *NEJM.* (121):351–356. Oct 1889. doi: 10.1056/NEJM188910101211502.

OPIOIDS

Strong Full Agonists

- Morphine
- Oxycodone
- Hydromorphone
- Fentanyl
- Methadone
- Meperidine

Weak Full Agonists

- Codeine
- Hydrocodone

Weak Agonist/Reuptake Inhibitor

- Tramadol

Full Agonist/Reuptake Inhibitor

- Tapentadol

Mixed Agonist/Antagonists

- Pentazocine
- Butorphanol
- Nalbuphine

Partial Agonist

- Buprenorphine
- Buprenorphine + Naloxone

U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products*. Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
The Medical Letter on Drugs and Therapeutics. Abuse-deterrent opioids. *JAMA*. 2019;319(19):2036-2037.

OPIOID RECEPTORS

Receptor	Activity
Mu (μ)	Analgesia Respiratory Depression Euphoria Miosis Reduced Gastric Motility Physical Dependence
Delta (δ)	Analgesia Respiratory Depression
Kappa (κ)	Analgesia Sedation Dysphoria Miosis Diuresis

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OPIOIDS – SAFETY CONCERNS

Controlled Schedule II EXCEPT Codeine which varies depending on product/dose

Risk Evaluation and Mitigation Strategy (REMS) REQUIRED for all opioids

- Prescriber education and counseling requirements

Monitor patients who are at high risk for respiratory depression

All opioids increase the risk of hypotension

U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products.* Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
The Medical Letter on Drugs and Therapeutics. Abuse-deterrent opioids. *JAMA*. 2019;319(19):2036-2037.

HOW MANY BLACK BOX WARNINGS ARE THERE FOR OPIOIDS?

OPIOIDS – BLACK BOX WARNINGS

Addiction, abuse and misuse can lead to overdose and death

Respiratory depression, which can be fatal

Use of any opioid with benzodiazepines or other CNS depressants, including alcohol, can increase the risk of death

Morphine ER capsules, Nucynta ER, Oxymorphone ER and Hydrocodone ER – do not consume alcohol with these medications as it can lead to overdose

Accidental ingestion/exposure of even one dose in children can be fatal

Crushing, dissolving or chewing of the long acting products can cause the delivery of a potentially fatal dose

Life-threatening neonatal opioid withdrawal with prolonged use during pregnancy

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SELECTING OPIOIDS

Route of Administration

Short Acting Vs. Long Acting

Opioid Naïve Patients Vs. Opioid Tolerant Patients

Patient Specific Factors

- Kidney function
- Liver function
- Prior use
- History of abuse
- Cause of pain

Side Effect Profile of Opioids

Chronic Therapy Patients

- Obtain informed consent
- Obtain management agreement

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FORMULATIONS

Oral	Intravenous	Intramuscular	Subcutaneous
Transdermal	Lozenge	Buccal Film	Sublingual Tablets
Buccal Tablet	Nasal Spray	Rectal	Patient Controlled Analgesic

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ORAL OPIOID FORMULATIONS

Opioid (generic name)	Short-Acting Formulation	ER/LA Formulation
Morphine	Solution (generic) Tablet (generic)	24-h ER capsule (Kadian, generic) 24-h ER abuse-deterrent capsule (Embeda) 12-h ER abuse-deterrent tablet (MorphaBond ER,) ER tablet (generic, MS Contin) 12-h ER tablet abuse-deterrent (Arymo ER)
Oxycodone	Capsule (generic) Solution (generic) Tablet (Roxicodone, generic) Tablet abuse-deterrent (RoxyBond, Oxaydo)	12-h ER abuse-deterrent capsule (Xtampza ER, Torxyca ER) 12-h ER abuse-deterrent tablet (generic, OxyContin, Targiniq ER)
Hydrocodone		12-h ER abuse-deterrent capsule (Zohydro ER) 24-h ER abuse-deterrent tablet (Hysingla) 12-h ER abuse-deterrent tablet (Vantrela ER)
Hydromorphone	Solution (generic, Dilaudid) Tablet (generic, Dilaudid)	24-h ER abuse-deterrent tablet (generic, Exalgo)
Oxymorphone	Tablet (generic, Opana)	12-h ER abuse-deterrent tablet (Opana ER) 12-h ER tablet (generic)

U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products.* Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
The Medical Letter on Drugs and Therapeutics. Abuse-deterrent opioids. *JAMA*. 2019;319(19):2036-2037.

WHICH OPIOIDS ARE AVAILABLE AS PATIENT CONTROLLED ANALGESIA?

U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products.* Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
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PATIENT CONTROLLED ANALGESICS (PCA)

Useful for patients with extremely severe pain which requires constant doses of opioid medications

Narcotic delivery where the patient self-administers narcotics by using a preprogrammed mechanical infusion device

- Basal rate – Provides baseline analgesia and pain control
- Intermittent boluses – Provides analgesia for breakthrough pain
- Lock-out period – Prevents pump from delivering dose at every press of button
- Maximum dose/hour is limited

Administered through intravenous, subcutaneous, intrathecal or rectal routes

Avoids delays in administration by caregiver if patient is in immense pain

Gives patient a greater sense of control over the pain

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The Medical Letter on Drugs and Therapeutics. Abuse-deterrent opioids. *JAMA*. 2019;319(19):2036-2037.

SHORT ACTING VS. LONG ACTING

Short Acting

- Immediate Release
- Acute or "breakthrough" pain
- Short half-life ~ 2-4 hours
- Opioid naïve patients
- Oxycodone, Morphine IR, Hydromorphone

Long Acting

- Extended Release
- Maintenance therapy
- Longer half-life depending on product
- Reserve for more stable patients
- Methadone, Fentanyl Patches, Oxycodone ER, Morphine ER

U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products*. Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
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RENAL VS HEPATIC

Renal Issues

- Morphine metabolite (morphine-3-glucuronide (MG3)) – renally cleared – Myoclonus and agitation
- Preferred agents – Fentanyl and Oxycodone
- Hydromorphone has renal metabolites but much lower concentration than morphine

Hepatic Issues

- Oxycodone and Fentanyl patches both require dose adjustments for mild liver disease
- Preferred agent – Morphine

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Portenoy RK, Ahmed E. Principles of opioid use in cancer pain. *J Clin Oncol*. 2014;32(16):1662-1670.

OPIOID-RELATED SIDE EFFECTS

- Overdoses & Respiratory Depression
- Opioid-Induced Constipation (OIC)
- Nausea & Vomiting
- Drowsiness & Sedation
- Pruritis
- Opioid Induced Hyperalgesia
- Allergic Reactions

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OVERDOSES & RESPIRATORY DEPRESSION

Usually occurs if patient takes a higher dose than recommended or if there are issues with elimination from the body

Can be prevented if doses are titrated conservatively as higher accumulations occur with a substantial dose increase

Dangerous if respiratory rate falls below eight breathes/minute

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OVERDOSES

Most states have been seeing decrease in overall deaths.

Younger age (35-44 years old) experience highest rate of deaths

Opioids, particularly illegally-made fentanyl, contribute the most to drug overdoses

Males are at greater risk than females

Race disparities have been increasing, Black and American Indian/Alaskan Natives have seen the highest increases in deaths

Lack of access to treatment increases the risk of deaths

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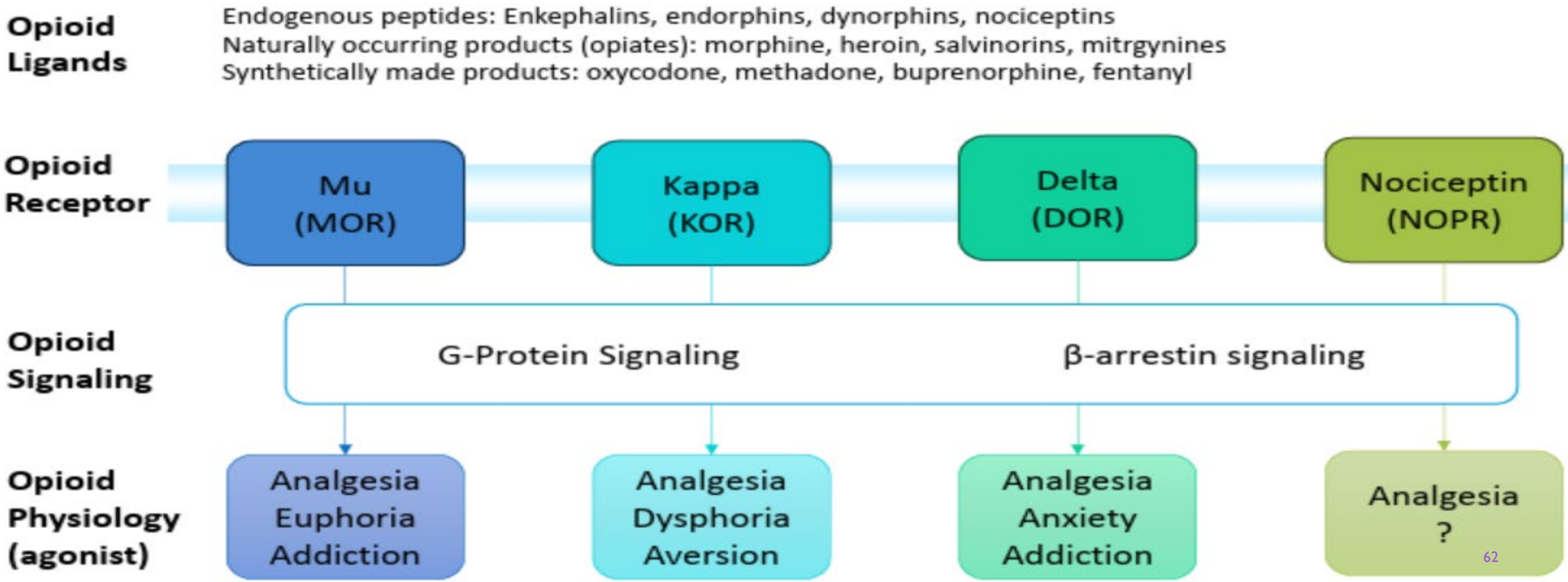
Portenoy RK, Ahmed E. Principles of opioid use in cancer pain. *J Clin Oncol*. 2014;32(16):1662-1670.

OVERDOSES



U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products*. Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
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WHAT RISK FACTORS INCREASES THE RISK OF A PATIENT BECOMING ADDICTED OR HAVING AN OVERDOSE?

OVERDOSES – RISK FACTORS

Changes in tolerance, this may include using after recent period of abstinence (ie, correctional or detox facility)

History of past overdoses

Using higher amounts or more potent drug

Having chronic health conditions such as, HIV, hepatitis C, lung disease, heart disease, or other health concerns

Changes in the drug supply

Mixing opioids with respiratory depressants or "downers," such as alcohol or benzodiazepines (benzos)

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OVERDOSES – TREATMENT

Naloxone (Narcan, Evzio auto injector, ReVive, Kloxxado)

- Semisynthetic opioid-receptor antagonist that reverses the clinical effects of opiate analgesics
- Available as nasal spray, injection or auto-injector
- May cause acute withdrawals in patients who are physically dependent on opioids

National Institute on Drug Abuse. January 2022. Accessed December 17, 2024. https://nida.nih.gov/publications/drugfacts/naloxone; FDA. Updated August 8, 2024.

Narcan

Emergent Biosolutions

- Two 4mg/0.1mL unit-dose nasal spray devices per pack
- FDA Approved Mar 29, 2023
- $41 package price (Aug 31, 2023)
- Available September 2023
- FDA News Release https://www.fda.gov/news-events/press-announcements/fda-approves-first-over-counter-naloxone-nasal-spray

RiVive

Harm Reduction Therapeutics

- Two 3mg/0.1mL unit-dose nasal spray devices per pack
- FDA Approved July 28, 2023
- $36 package price (Aug 31, 2023)
- Available Early 2024
- FDA News Release https://www.fda.gov/news-events/press-announcements/fda-approves-second-over-counter-naloxone-nasal-spray-product

Guideline	Recommendation
CDC Opioid Prescribing Guideline for Chronic Pain	"Clinicians should offer naloxone when prescribing opioids, particularly to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients with sleep-disordered breathing, patients taking higher dosages of opioids (eg, ≥50 mg equivalents/day), patients taking benzodiazepines with opioids, and patients at risk for returning to a high dose to which they have lost tolerance (eg, patients undergoing tapering or recently released from prison)."
NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain	"Discuss the role of naloxone for administration by caregivers in the event of respiratory depression and sedation and make available as indicated or as required by local and/or state regulations."
ASCO Guideline: Opioids for Cancer Pain.	"Consider prescribing naloxone to those receiving 50 morphine mg equivalents as a rescue resource if there is concern for unintended access of the opioid by children or vulnerable family members (eg, cognitively impaired persons). Consider naloxone also for patients receiving opioids with benzodiazepines, gabapentinoids, or other sedating agents."

CDC. November 3, 2022. Accessed December 17, 2024. https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm; NCCN. Clinical Practice Guidelines in Oncology. Adult cancer pain, version 3.2024. Accessed December 17, 2024. https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf; American Society of Clinical Oncology. J Clin Oncol. 2022;41(4):914-930.

ABUSE-DETERRENT OPIOIDS

Abuse-Deterrent Characteristics	Examples of Available Drug Products
Physical	
Resists nonoral abuse by forming a viscous gel when dissolved, difficult to break/crush	Oxycodone ER (OxyContin) Oxycodone IR (RoxyBond) Hydrocodone ER (Hysingla ER, Vantrela ER) Morphine ER (MorphaBond, Arymo ER)
Resists nonoral abuse by forming a viscous gel when dissolved	Hydrocodone ER (Zohydro ER)
Difficult to crush or inject	Oxycodone ER (Xtampza ER)
Crush resistant	Hydromorphone ER (Exalgo)
Agonist/antagonist combination	
Formulated with sequestered naltrexone that is released when dosage form is crushed or dissolved	Oxycodone ER/naltrexone (Targiniq ER; Troxyca ER) Morphine ER/naltrexone (Embeda)
Aversion	
Forms a viscous gel when dissolved; excipients cause nasal burning if snorted	Oxycodone IR (Oxaydo)

The Medical Letter on Drugs and Therapeutics. Abuse-deterrent opioids. *JAMA*. 2019;319(19):2036-2037.
Curfman GD, Beletsky L, Sarpatwari A. Benefits, limitations, and value of abuse-deterrent opioids. 2018. *JAMA Intern Med*. 2018;178(1):131-132.

OPIOID-INDUCED CONSTIPATION

- Most common adverse effect of chronic opioid therapy
- Opioids slow gastric emptying, decrease peristalsis and decrease secretion and blood flow in the gastrointestinal tract
- Symptom tolerance DOES NOT occur, meaning the patient may have constipation for as long as they are on opioids

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OIC TREATMENT

Laxatives

- Stimulant laxatives – senna or bisacodyl
- Osmotic laxatives - Miralax
  - Can add stool softener
- AVOID bulk-forming laxatives

PAMORAs – Peripherally-acting mu-opioid receptor antagonists

- Methylnaltrexone (Relistor)
- Naloxegol (Movantik)

Last Line

- Lubiprostone (Amitiza)

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PRURITIS

Most common with morphine and codeine

NOT an allergic reaction! It is considered an adverse reaction

Related to histamine release in the periphery

Treatment

- Change to another opioid
- Reduce dose of morphine/codeine
- Cool compresses
- Antihistamines

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ALLERGIC REACTIONS

Cross reactivity between opioids is common

If allergic to morphine, can easily cross to hydromorphone, codeine, hydrocodone and oxycodone

Treatment

- Fentanyl
- Methadone
- Tramadol

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WITHDRAWALS

Physiologic response to abrupt discontinuation

Usually occurs in patients who are physically dependent

Symptoms are unpleasant but rarely life-threatening

Treatment

- Clonidine
- Hydroxyzine
- Methadone
- Buprenorphine

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NEUROPATHIC PAIN – TREATMENT

Drugs	FDA-Approved Pain Management Indications	Counseling Points
Tricyclic antidepressants •Amitriptyline •Nortriptyline •Desipramine	None	Anticholinergic adverse effects are common, particularly among older patients (drowsiness, blurred vision, dizziness, urinary retention, confusion, dry mouth, constipation)
Serotonin norepinephrine reuptake inhibitors •Duloxetine •Venlafaxine •Milnacipram	Chronic musculoskeletal pain (duloxetine) Fibromyalgia (duloxetine, milnacipran) Diabetic peripheral neuropathy (duloxetine)	Nausea is most common adverse effect May increase blood pressure May increase bleeding risk, especially in combination with NSAIDs
Gabapentinoids •Gabapentin •Pregabalin	Postherpetic neuralgia (gabapentin, pregabalin) Fibromyalgia (pregabalin) Diabetic peripheral neuropathy (pregabalin) Neuropathic pain associated with spinal cord injury (pregabalin)	Dizziness and drowsiness are most common adverse effects, may need to titrate slowly due to drowsiness May cause peripheral edema

Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: systematic review, meta-analysis and updated NeuPSIG recommendations. *Lancet Neurol*. 2015;14(2):162-173.
U.S. Food and Drug Administration. *Drugs@FDA: FDA Approved Drug Products*. Product labeling for individual drugs and drug products. 2018. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. *Lancet Neurol*. 2010;9:807-819.

PAIN MANAGEMENT
ARE OPIOIDS THE BEST OPTION?

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