The Art of Pain Management

Anna Arabyan, PharmD

Financial Disclosures

- Board Member
  - Alzheimer's Care Armenia
- Shareholder
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- Employee
  - Generation Care
  - University of Southern California

Pain, the Universal Problem

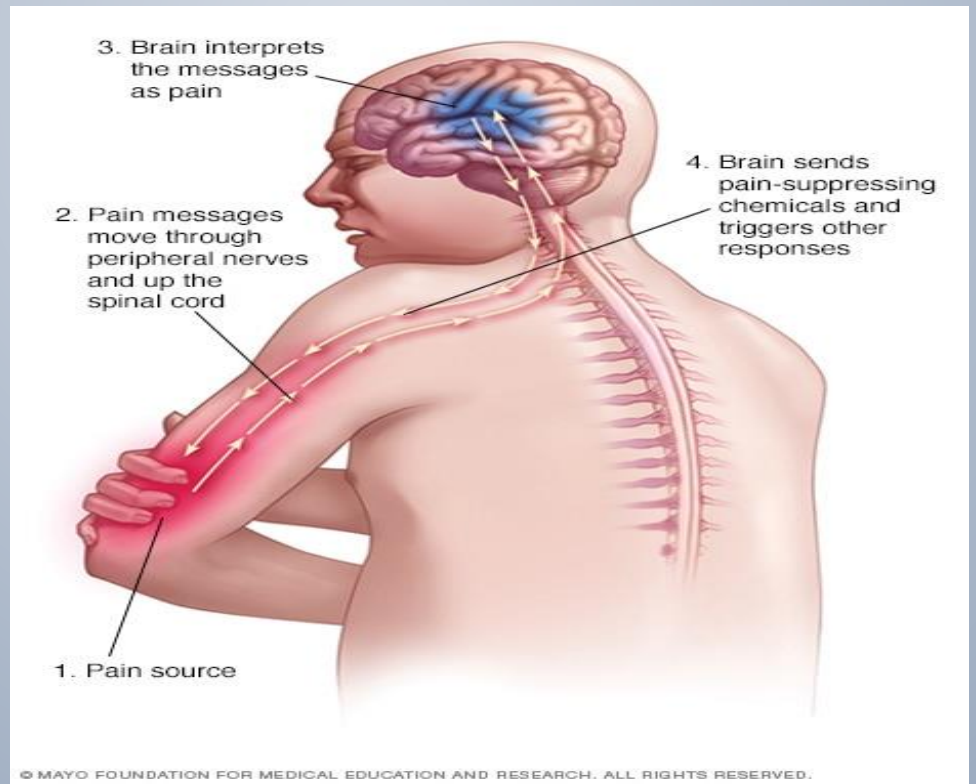
- Pain engages us at an **Emotional Level**
- Pain plays a **protective** role for survival
- It sends a signal that nature assures we cannot ignore.
- We focus attention on the affected area and marshal our resources to prevent further injury.
- Pain Illustration by Rene' Descartes
  - Reflexively withdraw foot
  - Avoid situation in the future
  - Limit activity, enabling healing to occur

Fellers J.C. (2016) Theories of Pain and Addiction: Type of Pain, Pathways to Opiate Addiction. In: Matthews A., Fellers J. (eds) Treating Comorbid Opioid Use Disorder in Chronic Pain. Springer, Cham

What is Pain?

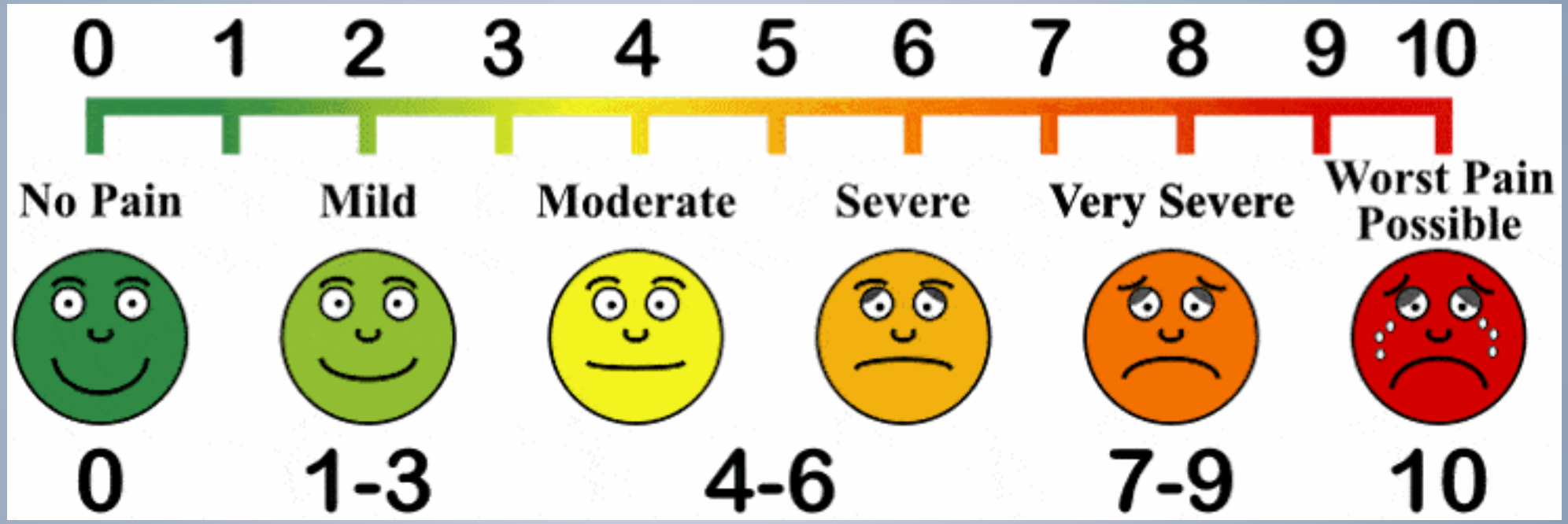
- **Acute pain** is a severe or sudden pain that resolves within a certain amount of time. You might feel acute pain when you have an illness, injury or surgery.
- **Chronic pain** is persistent, lasting for months or even longer. Chronic pain is considered a health condition in itself.

Pain is what the patient says it is. It's Subjective.



https://www.mayoclinic.org/understanding-pain

The Pain Scale



Pain is a Diagnosis and a Symptom

- Headache.
- Postsurgical pain.
- Post-trauma pain.
- Lower back pain.
- Cancer pain.
- Arthritis pain.
- etc.

Types of Pain

THREE MAIN TYPES OF PATHOPHYSIOLOGY
can be considered to result in chronic pain[1]

Pain related to ***damage*** **of somatic or visceral tissue,** due to trauma or inflammation

NOCICEPTIVE PAIN

Examples:
Rheumatoid arthritis, osteoarthritis, gout

Pain related to ***damage*** **of peripheral or central nerves**

NEUROPATHIC PAIN

Examples:
Painful diabetic peripheral neuropathy, postherpetic neuralgia

Pain ***without identifiable nerve or tissue damage,*** hypothesized to result from persistent neuronal dysregulation—may be called

SENSORY HYPERSENSITIVITY

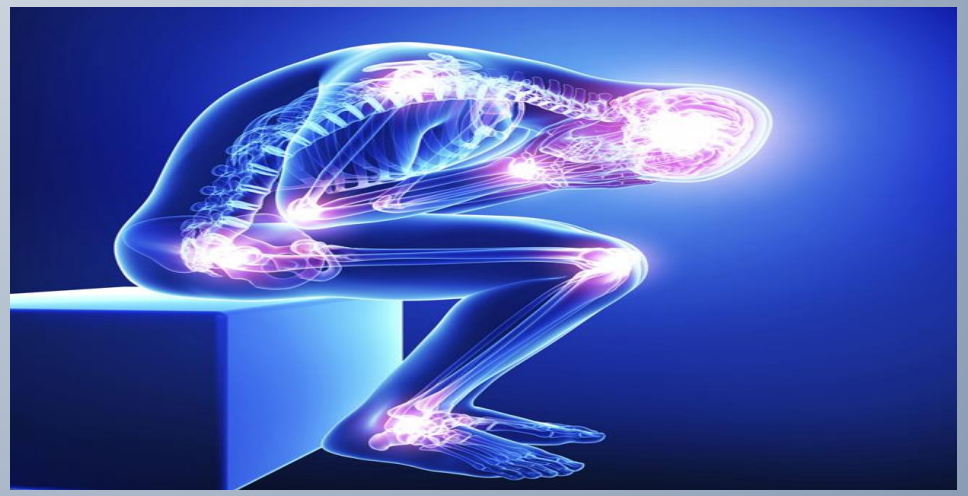
Example:
Fibromyalgia

More than 1 type of pain may be present in a given patient

http://www.rethinkopioids.com/pathophysiologic-types-of-chronic-pain

Where there is life, there is pain

- Pain affects more Americans than diabetes, heart disease and cancer combined.
- Pain is cited as the **most common reason** Americans access the health care system.
- Leading cause of disability and it is a major contributor to health care costs.



https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=57

Social Pain

- Social pain is caused by events such as feeling excluded from social connections or activities, rejection, bullying, the sickness or death of a loved one, a romantic break-up.
- Tedx: Social Pain is Real Pain
- https://www.youtube.com/watch?v=pRgxqBw-0pE

How Do We Know Social Pain Hurts?

- Depression Hurts: Associated with somatic symptoms such as general body pain
- Question: Does social/psychological pain activate these same areas, dorsal anterior cingulate cortex (dACC) and the anterior insula (AI)?
- Method of the Study:
  - Participants stay still in the fMRI scanner
  - Researchers had them play “Cyberball”
  - Sometimes included in the game, sometimes excluded
  - Exclusion associated with increased activation in the dACC and the AI

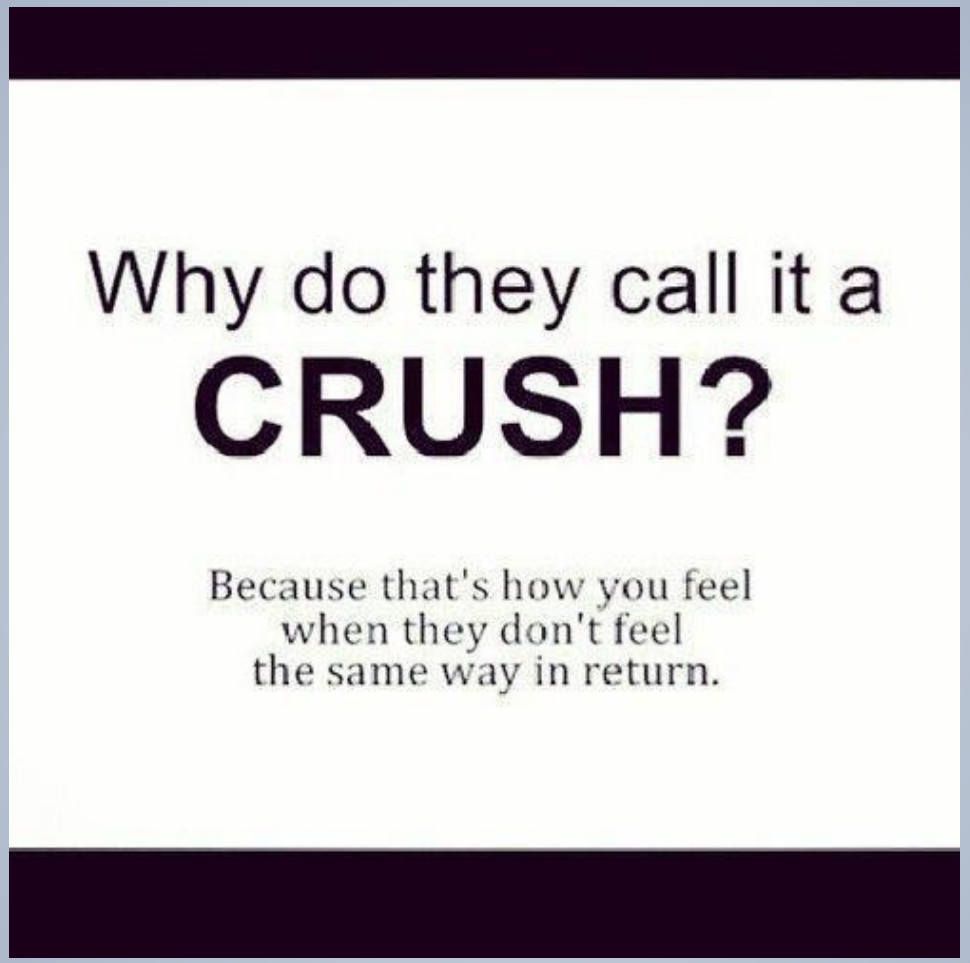
1.Trivedi, M. H. (2004). The Link Between Depression and Physical Symptoms. Primary Care Companion to The Journal of Clinical Psychiatry, 6(suppl 1), 12–16.
2. Eisenberger, N. I. (2012). Psychosomatic Medicine, 74(2):126-135.

Tylenol and Opiates

- Participants taking Tylenol over 3 weeks, reported feeling less hurt than those taking placebo
- Tylenol showed less activation in the dACC and AI to social rejection vs placebo
- Reduction in “isolation calls” in mice taking opiates

1. DeWall CN, MacDonald G, Webster GD, Masten CL, Baumeister RF, Powell C, Combs D, Schurtz DR, Stillman TF, Tice DM, Eisenberger NI. (2010). Acetaminophen reduces social pain: Behavioral and neural evidence. Psychol Sci. 21:931–7.
2. Eisenberger, N. I. (2012). Psychosomatic Medicine, 74(2):126-135

Why Does Rejection Hurt so Bad



https://www.ted.com/talks/jia_jiang_what_i_learned_from_100_days_of_rejection#t-917807

How Do We Know They Felt Rejected?

- ASK THEM!
- The greater the self reported “rejection”
- The greater the activity in dACC and AI
- Other studies have found that people have different sensitivities to social pain.
- The G allele
  - More sensitive to physical pain, need more morphine
  - More sensitive to social pain, more dACC and AI activation

1. DeWall CN, Masten CL, Powell C, Combs D, Schurtz DR, Eisenberger NI. (2012). Does the pain of rejection depend on attachment style? An fMRI study. Soc Cogn Aff Neuro.
2. Coulbalt L, Beaussier M, Verstuyft C, Weikmans H, Dubert L, Trégouet D, et al. (200). Environmental and genetic factors associated with morphine response in the postoperative period. Pharmacogenet Gen. 79:316–24.
3. Way BM, Taylor SE, Eisenberger NI. (2009). Variation in the mu-opioid receptor gene (OPRM1) is associated with dispositional and neural sensitivity to social rejection. P Natl Acad Sci. 106:15079–84.

Is There a Benefit to This Pain?

- Rejection served a vital function in our evolutionary past.
- Ostracized from our tribes was akin to a death sentence
- Advantage: experience rejection as more painful (i.e., because rejection mimicked physical pain in their brain)
- We would like to do without pain and yet without it we wouldn't be able to survive.

G. Novembre, M. Zanon, G. Silani. **Empathy for social exclusion involves the sensory-discriminative component of pain: a within-subject fMRI study**. *Social Cognitive and Affective Neuroscience*, 2014; DOI: 10.1093/scan/nsu038

A Review of Pain

- Biopsychosocial Model: pain is more than a biological phenomenon
- The mind–body connection between pain and psychological factors
- Emotional distress may predispose to and perpetuate pain
- Anxiety, depression, and anger are among the negative affect states involved in pain perception.
- Opioid medications can lessen psychiatric symptoms
- Prior to modern antidepressants, opiates were commonly used to treat depression.
- Pain is a uniquely individual experience

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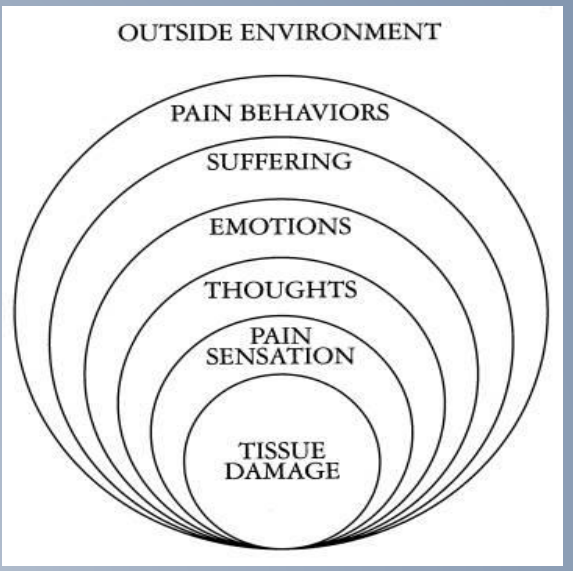
Risk Factors for Chronic Pain Among Adults

Factors associated with chronic pain.

Modifiable	Pain
	Mental health
	Other co-morbidities
	Smoking
	Alcohol
	Obesity
	Physical activity/exercise
	Sleep
	Nutrition
	Employment status and occupational factors
Non-modifiable	Age
	Sex
	Cultural background
	Socioeconomic background
	History of trauma/injury/interpersonal violence
	Heritable factors (including genetic)

Van Hecke O, Torrance N, Smith BH. Chronic pain epidemiology - where do lifestyle factors fit in?. *Br J Pain*. 2013;7(4):209–217. doi:10.1177/2049463713493264

Pain Catastrophizing



- Negative cognitive-affective response to anticipated or actual pain.
- An intensified emotional reaction to the pain experience to gain intimacy and closeness with others, and to solicit instrumental support
- It has been defined as “the tendency to magnify or exaggerate the threat value or seriousness of pain sensations”

Sullivan MJ, Thorn B, Haythornthwaite JA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain.* 2001;17(1):52-64.

How do we treat pain pharmacologically?

Non-Opioid Analgesics

- -NSAIDS
- -Acetaminophen

Antidepressants

- -Tricyclic Antidepressants
- -Serotonin Norepinephrine Reuptake Inhibitors

Antiseizure Medications

- -Gabapentin, Pregabalin, Others

PHARMACOLOGICAL TREATMENTS CONTINUED

Adjuvant Medications

- Topicals: NSAIDS, Lidocaine, Capsaicin
- Cannabis and Cannabinoids
- Botulinum Toxin
- Muscle relaxants (not recommended for chronic pain)
- Benzodiazepines (not recommended for chronic pain)

Opioids

Infusion Therapies

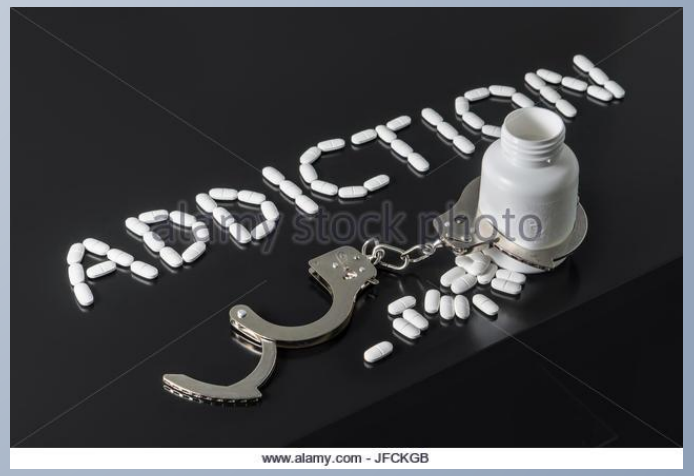
- Ketamine
- Lidocaine

Pharmacologic treatment based on type of pain[1,2]

Type of pain	First-line therapy	Considerations for opioid use
Nociceptive	NSAIDs	When other treatment options are inadequate, for pain severe enough to require potentially daily, round-the-clock, long-term treatment. Limit dose and duration whenever possible. Encourage as-needed use linked to meeting specific activity goals.
Neuropathic	Antidepressants (TCAs or SNRIs) or Antiseizure medications	
Central sensitization	Antidepressants (TCAs or SNRIs) or Antiseizure medications	Avoid whenever other multidisciplinary treatment options have not been systematically, sufficiently, and consistently trialed. Opioids often worsen central sensitization treatment outcomes.

Development of Opioid Addiction

- Healthcare providers may introduce patients to the effects of opioids when prescribing for painful medical conditions.
- This differs from how the initial exposure of many other potentially addictive drugs occurs.
- It has been recognized for some time that the risk for addiction with opioids is significant.



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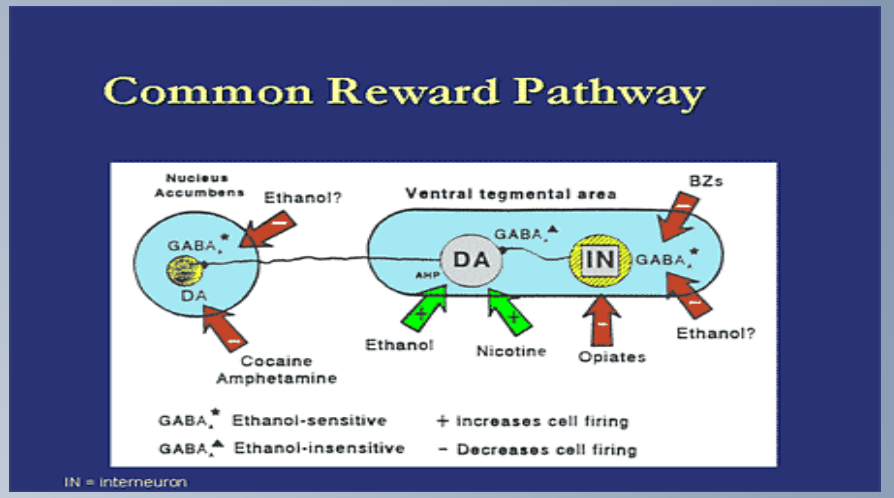
Opioids and Addiction



- Opioid drugs with abuse potential are agonists at the μ opioid receptor.
- This receptor is found in the brain, spinal cord, and intestinal tract.
- Acute activation of μ receptors leads to analgesia, mood changes including euphoria, sedation, meiosis, respiratory depression, and decreased gastrointestinal motility
- Opioid actions on the mesocorticolimbic **dopamine system.**
- Opioids facilitate dopamine release in the nucleus accumbens.

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Factors in Opioid Addiction

- As opioid dose was increased, the risk for addiction also increased
- The chronicity of treatment also was related to risk
  - Larger effect than the dose in determining risk.
- Since by definition, chronic pain treatment has no end-date, it represents a higher risk situation.
- Obtaining overlapping prescriptions from multiple providers and pharmacies.
- Taking high daily dosages of prescription pain relievers.
- Having mental illness or a history of alcohol or other substance abuse.
- Living in rural areas and having low income.

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Misuse vs Abuse

- **Drug misuse –** The use of prescription drugs without a prescription or in a manner other than as directed by a doctor, including use without a prescription of one's own; use in greater amounts, more often, or longer than told to take a drug; or use in any other way not directed by a doctor.
- **Drug abuse or addiction –** Dependence on a legal or illegal drug or medication.

https://www.cdc.gov/drugoverdose/prevention/index.html

Misuse vs. Abuse

Misuse:

Using legal drugs in the wrong way.

How?

- ✓ Taken more than prescribed
- ✓ Using without doctor knowing
- ✓ Using someone else's medicine

Abuse:

Using substances that are illegal & are not intended to be taken into the body.

Examples?

- ✓ Marijuana
- ✓ Cocaine
- ✓ Heroin
- ✓ Other

Clinical Implications

- **Prescription drug monitoring programs (PDMPs) –** State-run electronic databases that track controlled substance prescriptions. PDMPs help providers identify patients at risk of opioid misuse, abuse and/or overdose due to overlapping prescriptions, high dosages, or co-prescribing of opioids with benzodiazepines.
- **Extended-release/long-acting (ER/LA) opioids –** Slower-acting medication with a longer duration of pain-relieving action.

CURES 2.0

https://www.cdc.gov/drugoverdose/prevention/index.html

A case example

38-year-old man with chronic low back and leg pain

- • Involved in serious motor vehicle crash 3 years ago
- • Operated on by local orthopedic surgeon • Post-operatively was placed on PRN oxycodone
- • Physician is retiring, and he is referred to you for continuation of care
- • Reported opioid dose was oxycodone 15 mg, 5 times a day
- • He reports “fair” pain relief
- • Review of records unremarkable
- • Prescription Drug Monitoring Program (PDMP) report appropriate
- • Initial Urinary Drug Screen (UDS) was positive for oxycodone and oxymorphone

Questions

- What is the diagnosis?
- Should this be treated with opiates?
- Are there other non-opiate options?
- Is this patient appropriate, what are his risk factors for opiate misuse?
- If this patient is only getting FAIR relief, is that due to underdosing or is he tolerant and the opiates no longer work?
- Does he have other concerning medical issues, sleep disorder, anxiety, mood disorder, or new or worsening dx?

More Questions

- Is a UDS result showing oxycodone and oxymorphone in a patient taking only oxycodone appropriate?
  - Yes, the oxymorphone is a metabolite.
- Kevin is taking oxycodone 15 mg, 5 times a day. What is his MED (morphine equivalent)?
  - If Kevin is taking oxycodone 15 mg, 5 times a day, his MED = 112mg/D (Calculation: 15mg X 5 times a day =75mg, 75mg of oxycodone X 1.5 (conversion factor) = 112.5 mg morphine)
- Why does it matter?
  - Studies show issues with hyperalgesia from opiates with MED> 90.

Long Acting Opioids

- What are your dosing options?
  - Wean, convert to long acting. You need to ask about how the patient takes the medication—is he spreading it out over the day, or only taking it early or late in the day?
- What are the possible advantages / disadvantages to different options (short acting vs. long acting)
  - Long-acting opiates have less spike in blood levels and give a baseline level of pain control.

Opioid Tapering

50 MME/day:

- 50 mg of hydrocodone (10 tablets of hydrocodone/ acetaminophen 5/300)
- 33 mg of oxycodone (~2 tablets of oxycodone sustained-release 15 mg)
- 12 mg of methadone (<3 tablets of methadone 5 mg)

- Patient requested a dose reduction
- Total daily dose of opioids exceeds 50 maximum morphine equivalent (MME) without benefit
- Patient using opioids in combination with benzodiazepines
- Inability to achieve or maintain anticipated pain relief or function improvement despite reasonable dose escalation
- Patient experiences overdose or other serious adverse event or shows early warning signs for overdose risk (e.g., confusion, sedation or slurred speech)
- Persistent non-adherence with opioid treatment agreement or showing signs of substance use
- Deterioration in physical, emotional or social functioning attributed to opioid therapy
- Resolution or healing of the painful condition

Centers for Disease Control and Prevention. Pocket Guide: Tapering Opioids for Chronic Pain. www.cdc.gov/drugoverdose/pdf/clinical_pocket_guide_tapering-a.pdf.

Withdrawal Symptoms

Opioid withdrawal is characterized by signs and symptoms of sympathetic stimulation, due to decreased sympathetic antagonism by opioids

- Anxiety
- Hypertension
- Tachycardia
- Restlessness
- Mydriasis
- Diaphoresis
- Tremor
- Piloerection
- Nausea
- Abdominal cramps
- Diarrhea
- Anorexia
- Dizziness
- Hot flashes
- Shivering
- Myalgias or arthralgias
- Rhinorrhea
- Sneezing
- Lacrimation
- Insomnia
- Dysphoria
- Yawning

Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs. 2003;35(2):253-259. http://www.naabt.org/documents/COWS_induction_flow_sheet.pdf.

Opioid Tapering

- Decrease of 10 percent of the original dose per week. Some patients who have taken opioids for a long time might find even slower tapers easier. (CDC)
- Symptoms typically start 2-to-3 half-lives after the last opioid dose.
- Generally, opioid withdrawal is **not life-threatening** in patients who don't have significant comorbidities.
- Tapering Support
  - **Alpha Adrenegic Agonists:** Anecdotal evidence for clonidine or guanfacine
  - **Symptomatic Pain Treatments:** nonsteroidal anti-inflammatory drugs or acetaminophen.
  - **Other Medications:** medication to treat nausea and vomiting or diarrhea.
  - **Behavioral Health Support:** Psychosocial interventions may include cognitive behavioral therapy and interdisciplinary programs for chronic pain.

Centers for Disease Control and Prevention. Pocket Guide: Tapering Opioids for Chronic Pain. www.cdc.gov/drugoverdose/pdf/clinical_pocket_guide_tapering-a.pdf

Implications for the Healthcare Team

- **Non-opioid therapy –** Methods of managing chronic pain that does not involve opioids.
  - acetaminophen (Tylenol®) or ibuprofen (Advil®)
  - cognitive behavioral therapy
  - physical therapy and exercise
  - medications for depression or for seizures
  - interventional therapies (injections).
- **Non-pharmacologic therapy**
  - physical treatments (e.g., exercise therapy, weight loss)
  - behavioral treatments (e.g., cognitive behavioral therapy, meditation).

Combined acetaminophen, ibuprofen produces similar amount of pain relief as opioids in ED patients

Chang A, et al. *JAMA*. 2017;doi:10.1001/jama2017.16190.
Kyriacou DN. *JAMA*. Volume 318, Number 17, Pages 1655-1656.
November 7, 2017

ADD TOPIC TO EMAIL ALERTS

Andrew K. Chang

ED patients with acute extremity pain had neither clinically important nor statistically significant differences in pain reduction at 2 hours when receiving a single dose of ibuprofen and acetaminophen or several different combinations of opioids and acetaminophen, according to findings recently published in *JAMA*.

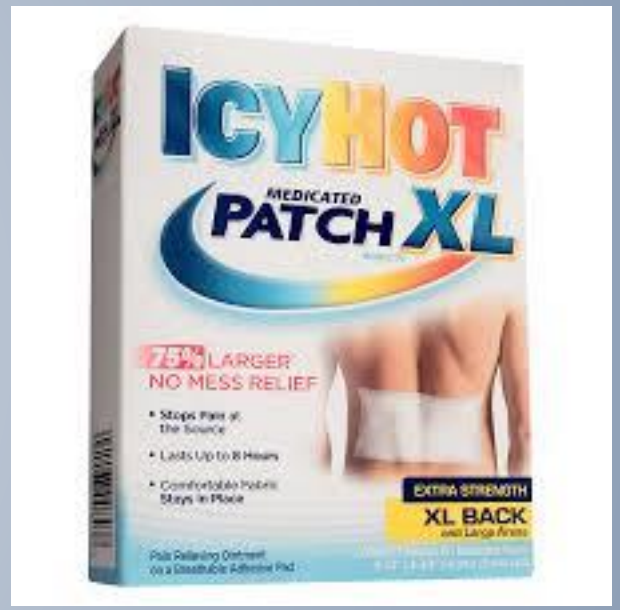
https://www.cdc.gov/drugoverdose/prevention/index.html

Proposed Solutions

- More than 125 million Americans suffering from either acute or chronic pain
- A huge need for the development of effective alternatives to opioids
- Enabled at least in part by a fuller understanding of the neurobiological bases of pain
- Best long-term solution for controlling and ultimately eradicating this epidemic
- Lower Dose Prescribing
- Decreased duration of treatment

Cold And Heat

- For certain types of injuries, the use of cold or heat may help dissipate pain.
- Not a large amount of scientific data to support the use of cold and heat but a helpful complement to other treatments.
- Cold, in particular, can be useful in the hours right after an injury.
  - Pain relief, decrease inflammation and muscle spasms and may help speed recovery.
- Heat may be useful for other types of injuries.
  - Raise pain thresholds and decrease muscle spasms in people suffering from osteoarthritis, useful for treating tendinitis early on, and may reduce back pain and disability.



Harvard.edu/blog/special-reports/pain-relief-natural-and-alternative-remedies-without-drugs-or-surgery

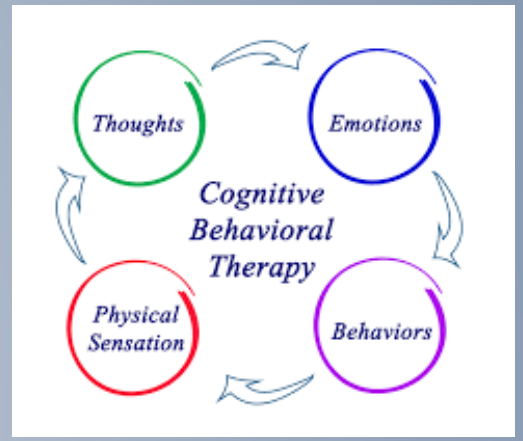
Exercise

- Helpful in common conditions: low back pain,arthritis, and fibromyalgia.
- Vicious cycle in which pain inhibits people from exercising for fear of causing more pain.
- Lack of exercise causes muscles to lose strength, making it even more painful and difficult to exercise.
- Staying physically active, despite some pain, can prevent that vicious cycle from starting—or at least keep it from accelerating.
- Physical activity also combats obesity, which is a risk factor for a variety of painful health conditions
- Physical activity releases endorphins, which can improve your mood

Harvard.edu/blog/special-reports/pain-relief-natural-and-alternative- remedies-without-drugs-or-surgery

Mind-Body Techniques

- Mind-body relaxation techniques have become well accepted as stress-reducing strategies. Help pain 2 ways:
- First, chronic pain conditions can rob people of a sense of control over their bodies and, thus, their lives. (CBT gives control)
- Second, they can help turn off what is known as the fight- or-flight response or the stress response.
- Cognitive behavioral therapy (CBT) is a form of psychotherapy that seeks to break counterproductive thought and behavior patterns that may worsen pain.
- Relaxation techniques emphasize a strong connection between the mind and the body and can calm revved-up muscle, metabolic, and hormonal responses.



Mindfulness

- Mindfulness meditation is another approach combining elements of relaxation and hypnotherapy, which seeks to increase focused attention and facilitate relaxation.
- Based in Theravada Buddhism, it seeks to increase intentional self- regulation to what is occurring in the present without attaching negative associations.
- As applied to pain management, a primary goal is to separate the pain sensation from unhelpful thoughts.

Is Marijuana Better Than Opioids?

- Medical marijuana may offer an alternative to addictive opioids.
- When researchers surveyed almost 3,000 medical cannabis users, they found that 30 percent had used opioids in the last 6 months.
- Of those respondents, 81 percent agreed or strongly agreed that marijuana was more effective alone than in combination with opioids.
- In addition, 97 percent said they agreed or strongly agreed that they could decrease their opioid usage when taking marijuana.

Marijuana For Pain Management

- Most marijuana-based products do not have approval from the United States Food and Drug Administration (FDA), and more evidence is necessary to confirm their safety and effectiveness.
- The different types of marijuana plants include the following:
  - *Cannabis indica (body)*
  - *Cannabis sativa (euphoria)*
  - hybrids
- There is limited research available on the use of specific marijuana strains for pain and other symptoms.
- Strain-specific recommendations are not medically proven.

Reiman, A., Welty, M., & Solomon, P. (2017, June 1). Cannabis as a substitute for opioid-based pain medication: Patient self-report. *Cannabis and Cannabinoid Research*, *2*(1), 160–166.

Thank You!

› annaarab@usc.edu