

Basic Principles, and Clinical Issues in Pain Management

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Prescribing Controlled Drugs:
Critical Issues and Common Pitfalls
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Disclosure/Disclaimer

- No conflicts to disclose
- The views and opinions expressed do not necessarily reflect those of the Alabama Board of Medical Examiners (ABME) or the Medical Association of the State of Alabama (MASA)

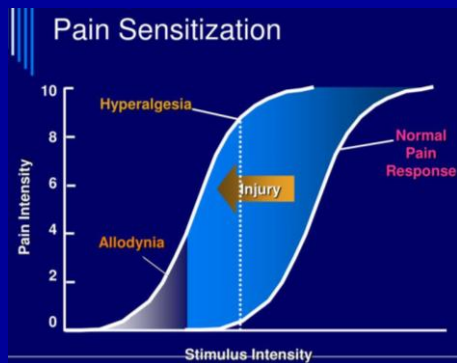
Goals

- Describe the neurophysiological processes involved in pain
- Outline the differences between acute and chronic pain
- Review the role of psychosocial factors in chronic pain and opioid effectiveness
- Illustrate clinical conditions, and the associated decision-making process

IASP Classification of Pain



Pain-related Terminology



Pain: Assessment

- The verbal expression of pain, is a behavior; considered to be 'part of pain', and not a verbal expression of it. It is **not a 1:1 correspondent** of the subjective experience of pain

Wittgenstein L. The Philosophical Review, 1958; 77, 3, pp. 275-320.
Galatano F. Pain and forms of life. Philosophical investigations on chronic pain. Esercizi Filosofici 6, 2011; 266-280

- "... the root problem may be neither the high risk or the low efficacy of long term opioid therapy but rather an **improper focus on reducing pain intensity**" (p.67) (Sullivan and Ballantyne. Pain, 2016, 157, 65-69)
- The pervasive use of the numerical pain rating (NPR) in the clinical setting **has been linked to the increase in opioid prescribing** (Farrar et al, 2001; Sullivan and Ballantyne, 2016).

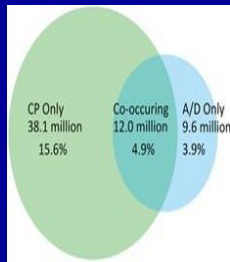
CP is not CP is not CP

- High vs low impact.
- Neuropathic vs Musculoskeletal
- Palliative vs Rehab/functional
- High vs low psych comorbidities
- Polymorphisms



Co-existing Chronic Pain and Anxiety/Depression: U.S. Adults: 2019 survey

- ~ 12 million (4.9% of population), co-existing chronic pain and A/D symptoms.
- Unremitted A/D symptoms co-exist in 23.9% of chronic pain vs 4.9% without chronic pain.
- Chronic pain co-exists in 55.6% of adults with unremitted A/D symptoms vs 17% without A/D symptoms.
- Co-existing symptoms associated with limitations in work, house-hold chores, and social activities.
- There is a need to target improving functional outcomes



De La Rose J, et al. Co-occurrence of chronic pain and anxiety/depression symptoms in U.S. adults: prevalence, functional impacts, and opportunities. PAIN, September 21, 2023. | DOI: 10.1097/j.pain.

Psychological/Cognitive Factors Affecting Pain Perception and Behavior

- **Pain appraisal:** The “meaning” attached to the pain, i.e. expected, accepted, punishment, badge of courage, disease conviction etc
- **Beliefs about pain:** Patient beliefs regarding the effect of pain on disability, function, emotions, need for medication, assistance for others, control over it
- **Coping:** Behavioral/cognitive responses to pain e.g. ignore, pray, relax, keep going, distract
- **Self-efficacy:** Patient beliefs that they and/or the strategies they apply will be effective



Depression

- S - Sleep
- I - Interest
- G - Guilt
- E - Energy
- C - Concentration
- A - Appetite
- P - Psychomotor retardation
- S - Suicide

Clinical Issues

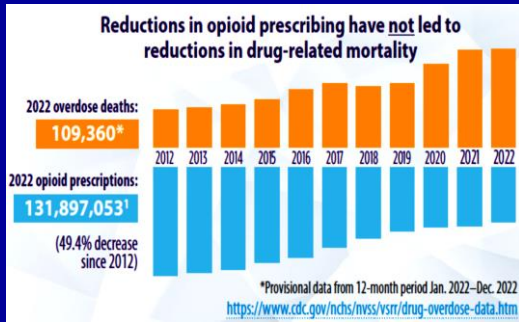
Chronic Pain: Growing Crisis

- Increase incidence
- Decrease availability of medication
- Decrease in prescribers/provides

Availability Affected By

- Production:
68% for oxycodone and 73% for hydrocodone reduction vs 2015
- Distribution
- Dispensing
- Coverage

Overdose Epidemic Report: 2023. AMA



Fentanyl Seizures: 2017- 2024

- US fentanyl seizures **increased by > 1700%** between 2017 and 2023
- **Total seizures: 66,303**, 67% in powder form, 33% pills.
- **Greatest number** in Florida, Arizona, and California
- California: greatest **number of pills** seized (n = 38.6 million), and greatest **weight of powder** seized (4315 kg).

JJ Palamar et al. National and regional trends in fentanyl seizures in the United States, 2017–2023 International Journal of Drug Policy. Available online 13 May 2024. 104417

AMA 2023 Recommendations

- Support patients with pain by following CDC's 2022 revised opioid prescribing recommendations and **rescinding arbitrary opioid prescribing dose and quantity thresholds, laws and policies**. Further support patients with pain by requiring health insurance companies and other payers to make non-opioid pain care alternatives more accessible and affordable, emphasizing social determinants of health, including transportation, housing, employment and other factors.

Overdoes Epidemic Report: 2023. AMA

Prescribing Dilemmas: What to Focus on

- **Guidelines:** inherently biased, multiple sources (federal, state, local), blatant assertion, lack longevity, e.g. **DSM 5TR**; 60% of panel shared in 14mill dollars-undisclosed industrial funding. 80% of psychiatric meds are prescribed by **primary care doctors**, -yet not represented proportionately
- **Safety:** side effects: physical including hormonal; psychosocial (diversion), SUD,
- **Effectiveness:** Pain, Qol, function, satisfaction
- **Evidence-based Medicine:** conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. Integrating the **experience** of the clinician, **values** of the patient, and the best available **scientific information**.

Questioning the Right to Pain Relief and its Role in the Opioid Epidemic

- Opioid prescribing: "... **the root problem** ... an improper focus on reducing pain intensity" (p.67) (Sullivan and Ballantyne. Pain, 2016, 157, 65-69)
- AMA, American College of Surgeons, The Joint Commission, AAFP, and CMS have **withdrawn their advocacy** of the "pain as the 5th vital sign" campaign. (Levy N, Sturgess J, Mills P. "Pain as the fifth vital sign" and dependence on the "numerical pain scale" is being abandoned in the US. Why? British Journal of Anaesthesia, 2018, 120 (3): 435-438)
- "To prevent further opioid epidemics we need to **abandon the clinical outpatient use of pain intensity scores** and redefine the medical necessity of pain treatment as **less about the reduction in pain intensity and more about the capacity to pursue personally values activities**." Sullivan MD, and Ballantyne JC. Mayo Clinic Proceedings. July 7, 2023

What Defines Good Pain Management?

- Patient report
- Significant-other report
- Reduction in Numerical Pain Rating
- Improvement in function
- MME/number of pills per day
- Practitioner comfort
- Adherence to a specific 'guideline'
- Absence of complaint

BZD: impact on cortical structure and function

- BZD: associated w/ **accelerated reduction in total brain volume**, e.g. hippocampus, amygdala, thalamus, regions involved in memory and mood regulation
- Chronic BZD: **may reduce neuroplasticity**, and the brain's ability to form new connections and adapt.
- **Benzodiazepine-induced neurological dysfunction (BIND)** (Ritvo AD, et al. Long-term consequences of benzodiazepine-induced neurological dysfunction: A survey. PLoS One. 2023 Jun 29;18(6):e0285584. doi: 10.1371/journal.pone.0285584.)
- **Protracted Withdrawal Syndrome (PWD)** (Ashton H. Protracted withdrawal syndromes from benzodiazepines. J Subst Abuse Treat. 1991; 8: 19-28).
- **Protracted Absence Syndrome (PAS)** (Manhapa et al 2018)

Gallie, Q. et al. Benzodiazepine use and neuroimaging markers of Alzheimer's disease in nondemented older individuals: an MRI and 18F-Flortaucipir PET study in the MEMENTO cohort. *Neuropsychopharmacology*. 48: 1114-1120 (2023). <https://doi.org/10.1093/napn/nnab011>

Post-op opioid use

- 900 patients filled a prescription
- **Oxycodone**: most commonly prescribed opioid (70%).
- 341 patients (28%) **did not** fill the prescription
- 191/900 (21%) **did not take** any of the medication.
- 252/900 (28%) **did not know how to dispose of the unused opioid tablets**
- Two studies found **73% and 77% patients did not secure unused opioids** (Bicket et al, JAMA Surgery, 2017, August 2, published online)

Unpublished data. 2023

Opioids and Children: "1 Pill Can Kill"



- Hospitalizations for prescription opioid-related poisonings increased **165%** for children ages 1-19, between 1997-2012
- Prescription opioid poisoning among adolescents 15-19 years increased by **176%**
- The largest percentage increase poisonings was among the 1-4 year by **205%**.
- Majority of the poisonings are **unsupervised ingestions**; of an opioid prescribed for a family member

Gaither et al. National trends in hospitalizations for opioid poisonings among children and adolescents: 1997 to 2012. JAMA Pediatrics. Published Online: October 31, 2016. doi:10.1001/jamapediatrics.2016.2154

Opioid Therapy: Be Aware of Opioid Induced...

Disorder	Incidence	MOA
Neurotoxicity	15% Ca pain study	Neuroexcitatory metabolites, e.g. morphine-6-glucuronide,oxymorphone-3-glucuronide; NMDA activity
Endocrinopathies	21-86%	Hypothalamic-pituitary-gonadal system
Hyperalgesia	Rare-27%	central glutaminergic system, spinal dynorphins, descending facilitation, genetic mechanisms, and decreased reuptake and enhanced nociceptive response
Immunosuppression	Unknown	impaired immune system function by affecting the H-P-A system, and suppressing natural killer (NK) cells

Ackerman WE. Periosteal opioid-induced pain and hyperalgesia. J Ky Med Assoc. 2006; 104:419-23.
 Marudhai S, et al. Long-term opioids linked to hypogonadism and the role of testosterone supplementation therapy. Cureus. 2020 Oct 5;12(10):e10813. doi: 10.7755/cureus.10813-10. PMID: 32178522. PMCID: PMC7642369.
 Matzo M, Dawson KA. Opioid-induced neurotoxicity. Am J Nurs. 2013 Oct 13;113(10):51-6. doi: 10.1097/01.NAJ.0000433351.53534.83. PMID: 24067633.
 Godwin B, et al. Identification and management of opioid-induced neurotoxicity in older adults. Can Fam Physician. 2022; 68(4): 269-270.

Chronic Pain and Neuroimmune Interface

- **Elevated levels of several cytokines** found in the CSF of patients with LDH and those with DDD, indicating neuroimmune activation
- **No of systemic inflammation** and signs of a communication between CSF and serum.
- Systemic expression of inflammatory proteins suggest a hypoinflammatory environment
- **Disease-specific** associations were found between cytokines in CSF and back pain intensity.

Rosenström A, et al. Unraveling the neuroimmune interface in chronic pain—the association between cytokines in the cerebrospinal fluid and pain in patients with lumbar disk herniation or degenerative disk disease. PAIN. 2024;165(7): e6-e16. July 2024.

Chronic Pain: Elderly & Cognitively Impaired



Altered:

- **Central processing:** altered functional connectivity and impaired contextual appraisal
- **Expression**
- **Affective response**
- **Response to opioids:** disruption of expectancy due to cognitive impairment (Benedetti et al. Pain, 2006; Cole et al. Eur J Pain, 2011)
- **Homeostenosis:** impaired ability to compensate/adapt (Karp et al. Brit J Anes, 2008, 101)
- **Consequence:** increased mortality and dementia (Domenichiello AF, Ramsden CE. Prog Neuropsychopharmacol Biol Psychiatry, 2019 :93:294-299.

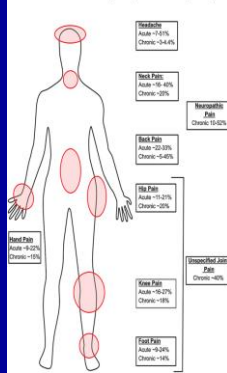
Chronic Pain in Elderly: Beliefs and Fears

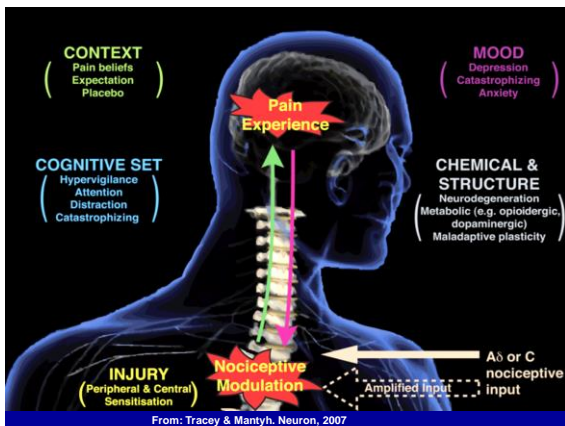
Pain is a normative part of aging. Develop fatalistic attitudes about enduring pain and dysphoria.

Reasons for not 'speaking out':

- (1) Fear of being labeled a bad patient
- (2) Pain may signify serious illness
- (3) Fear of addiction
- (4) Pain medications need to be saved 'for the end'
- (5) Fear of lose of independence
- (6) Anxiety over additional diagnostic tests and the cost of such tests

Prevalence of Pain in Adults aged 65 years or older by site of pain





Regarding the Use of Opioids



Courtesy: Dr. David McLain

Pain is not an opioid deficiency

Life is not a chemical deficiency

Don't say yes if you cannot say no

Be the clinician your patient needs; not just the one they want

Be a responsible prescriber, and not a 'vending machine'

Thank You

