



Pain, The Brain, & Opioids



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Disclosures

- Salix Drug Development Advisory Board, summer 2019 (OIBD and Opioid Abstinence)

Objectives

- To promote objective, evidence-based critical thinking regarding the role of opioids for the treatment of intractable, debilitating pain
- Help attendees recognize prescribing biases and acknowledge the influence these have on their opinions, decisions, and practices
- To improve patient health, function, and life experience

Audience Participation

Text your response to the question posed to:
801.573-7697

What Do You See?



What Do You See? A Chronic Pain Epidemic? An Opioid Epidemic?



KEY QUESTIONS

Debilitating Pain

Millions of Americans
\$600 - 800 Billion

Substance Abuse

Millions of Americans
\$750 Billion

Of the 40+ Million Americans with Chronic Pain and the 10 Million Americans on Chronic Opioid Therapy:

- What is Actually Prescribed, to Whom, and How Much?
- How Much Dose Escalation Occurs Over Time?
- Who Benefits, Who Is Harmed and How Do We Predict?
- How Do We Prevent Morbidity/Mortality from CP and COT

Imperfect Construction: A Problem of Coherence



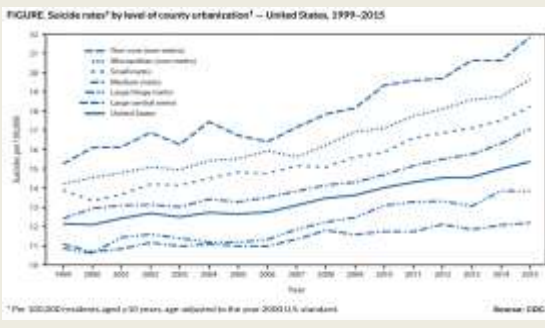
The climate science analogy

- As in climate science, failing to understand, acknowledge and work on root causes of an issue leads to frustration, failure and futility. In the dual "epidemics" of chronic pain and substance misuse/abuse, we have only been presented with the equivalent of real time weather maps, while being asked to predict in advance and prevent the imminent ravages of a class 5 hurricane, a major flood, or drought-related famine.
- HOPEFULNESS & DEATHS OF DESPAIR: What is CAUSE and what is the EFFECT?

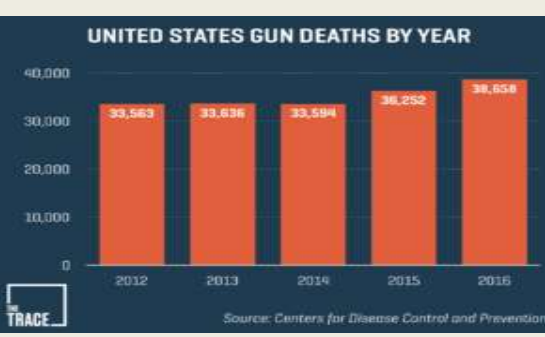


UNIVERSITY OF UTAH HEALTH, 2017

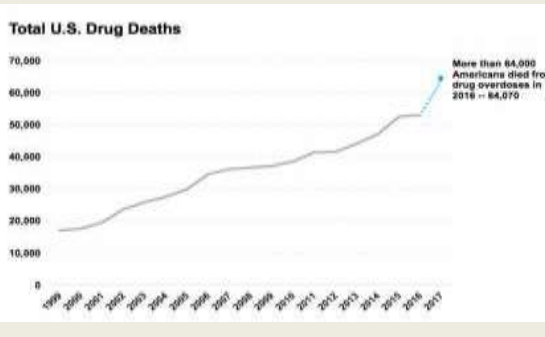
HOPELESSNESS AND DEATHS of DESPAIR: Decline in mental health



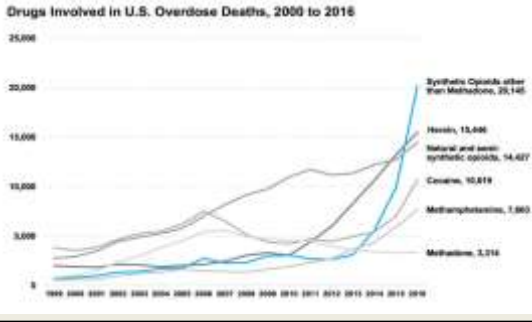
HOPELESSNESS AND DEATHS of DESPAIR: Fears for personal safety



HOPELESSNESS AND DEATHS of DESPAIR: Rise in substance misuse and abuse

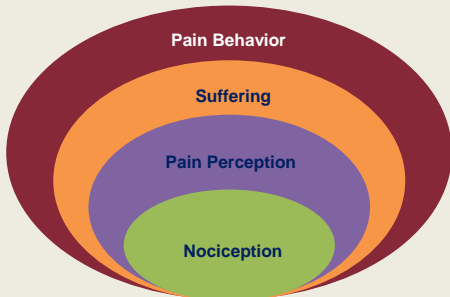


HOPELESSNESS AND DEATHS of DESPAIR: Rise in high risk substance abuse

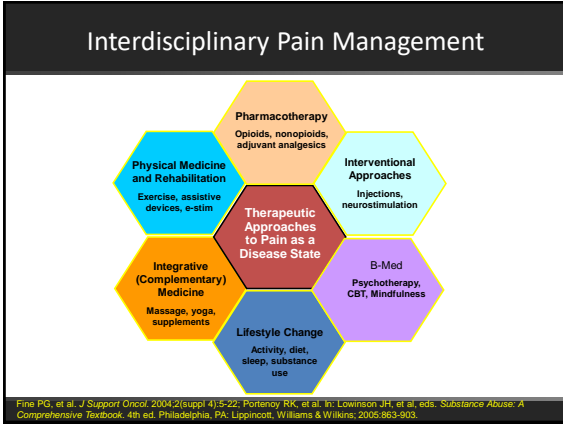


"We shall not cease from exploration, and the end of all our exploring will be to arrive where we started and know the place for the first time."
T.S. Eliot (1888-1965)

The Complex Nature of Pain



Adapted from: Loeser J, et al. *Bonica's Management of Pain*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins. 2001:241-254.

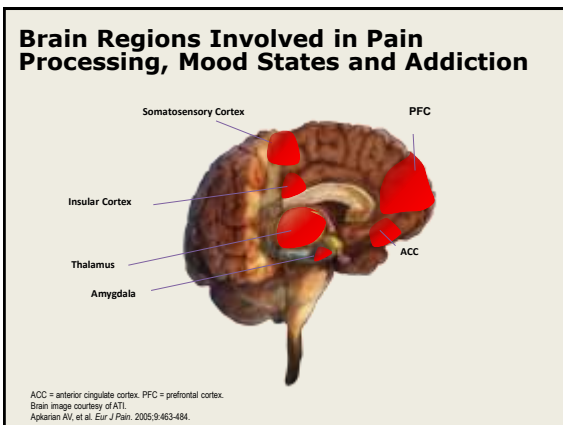


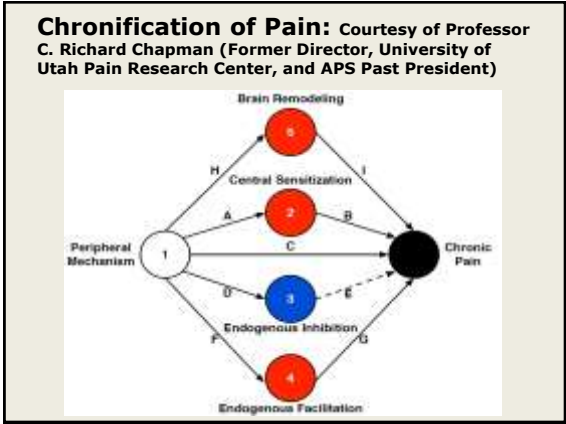
Genetics and Epigenetics of Chronic Pain States and Addiction

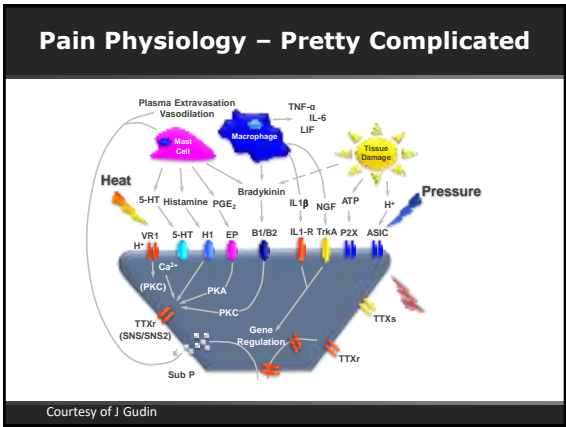
- Genetic factors can explain a significant amount of the variability in the perception of pain and drug liking.
- Recent evidence suggests a role for polymorphisms of genes in the serotonergic, dopaminergic and catecholaminergic systems in the pathogenesis of chronic pain and addiction
- Environmental factors may trigger the development of these disorders in genetically predisposed individuals.

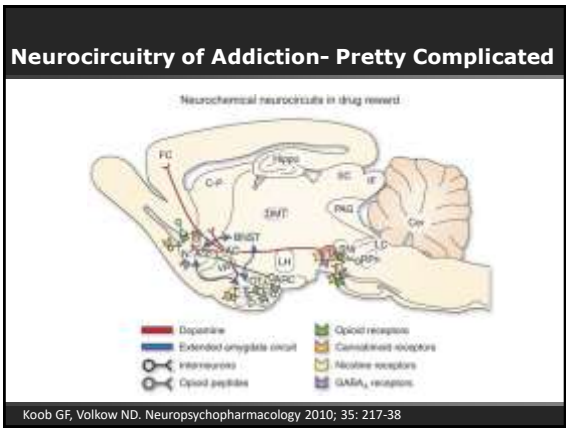
de Andrade D C, et al. Epigenetics insights into chronic pain. Pain, 2017; 158(8):1473-1480.

Cecil CAM et al. Epigenetics of addiction: Current knowledge, challenges, and future directions. J Alcohol and Drugs, 2016; 77(5), 688-691









People/Patients – More Complicated..



What Clinicians See

- Patients who use opioids responsibly over time
- Patients with co-morbid pain and substance abuse disorders
- Non patients/ abusers who obtain opioids for illicit purposes



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Pain: A Flow Chart



FIGURE 3-4 The picture of pain.
 NOTE: People can move between and among these groupings and can fit in more than one group (simultaneously). Standard color-coding represents similar categories (e.g., for those with chronic pain, the blue boxes are for those with chronic or acute pain).
 Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Institute of Medicine of the National Academies of Science, Medicine and Engineering.

Vulnerability to Opioid Addiction

Individuals respond differently to opioid exposure

No addictive disease with exposure

Addictive disease after opioid exposure

No addictive disease due to lack of exposure

L Webster 28

Population of Rx Opioid Users is Heterogeneous

Addicted (SUD) Substance Abusers Recreational Users Self-Treaters Adherent Chemical Copers Substance Abusers Addicted (SUD)

Non-medical Users Pain Patients

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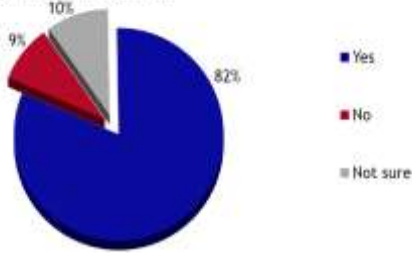
20 years of expanded opioid prescribing

- What have we learned?
 - Something fundamental about opioid pharmacology?
 - Something fundamental about the interface of people and opioids?
 - Something fundamental about the problems of our health care system?

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Americans Believe Using Pain Killers Can Result in Addiction

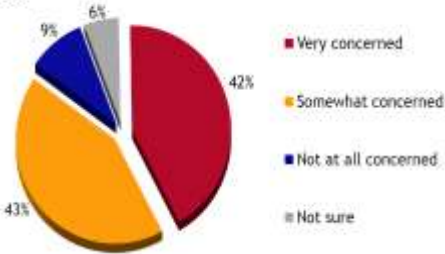
Do you think that taking prescription painkillers for long-term, chronic pain could result in addiction?



Source: A Research America poll of U.S. adults conducted in partnership with Data Insights in March 2017.

85% Say They're Concerned About Misuse of Medication

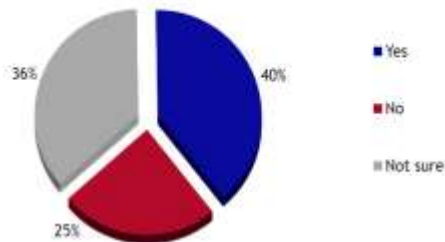
How concerned are you that prescription pain medication can be abused or misused?



Source: A Research America poll of U.S. adults conducted in partnership with Data Insights in March 2017.

Only One-Fourth Say Abuse, Addiction Not a Major Problem in Their Community


Is prescription pain medication abuse and addiction a major problem in your community?



Source: A Research America poll of U.S. adults conducted in partnership with Data Insights in March 2017.

Opioid Associated Deaths – Why???

- **Over-Prescribing (Physician)**
 - Dose escalation too rapid
 - Starting dose too high
 - Over reliance on conversion tables
 - Inadequate risk assessment
- **Non-Adherence (Patient)**
 - To control pain
 - To "cope"
 - Substance abuse
- **Unanticipated co-morbidities**
 - QT prolongation
 - Pharmacogenetics and methadone metabolism
 - Sleep disordered breathing
- **Misaligned Incentives and Systems**
 - Interdisciplinary Care Model with risk management is the rare exception
 - Pain education and research still lacking
 - No insurance standards or requirements



Fine's Dictum

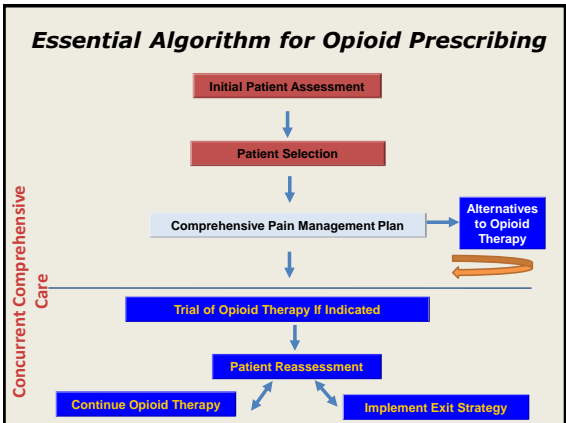
- The polemic of "pro-opioid" and "anti-opioid" is a false one, and serves neither the practitioner, the patient or society well. The ethical clinician is "pro-health", and makes treatment decisions with her/his patient within that context.
- Until such time that there is a class of drugs as efficacious and versatile as the opioids, clinicians need to learn how to select patients for opioid therapy, when indicated, and manage them as safely and effectively as possible.

Cum Scientia Caritas

❖ **All medication management must be tailored to the individual patient's needs and circumstances. Ongoing critical thinking, sound judgment, and clinical experience can never be replaced by formulae.**

Patient Selection: Indications for Opioid Therapy

- Persistent, debilitating levels of pain despite reasonable trials of less risky forms of therapy, including non-opioid analgesics and adjuvants
 - or
- Pain severe enough to require rapid relief
 - or
- Patient characteristics contraindicate use of other analgesics
 - and
- Benefits of opioid therapy are likely to outweigh harms based upon comprehensive assessment including risk evaluation



HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics (Oct. 2019)

https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf

Oh, the wonder of it all...