Pain Management and Opioid Therapy 2022: New Guidelines

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Objectives:

- Develop an understanding of the newer guidelines and position statements and their emphasis on balancing management of pain with risks associated with opioids
- Gain knowledge in the risk assessment of the chronic pain patient and the appropriate management of those patients in a multi-modal treatment plan
- Understand the implications of SB 1446 and 848 in the management of the acute and chronic pain patient and how it impacts your practice

Unintended Consequences Addressed by 2022 Guidelines

- Forced opioid tapering
- FDA warning: "Serious harm"
- Patient abandonment and fumbled handoffs
- Increase in "over" referrals
- Reduction in physicians willing to prescribe
- Stigma associated with opioids
  - Patient and physician
- Suffering, suicide and disability

2022 CDC Guidelines: Focus

- Not a replacement for clinical judgment and emphasizes individualized patient care
- Not intended to be applied as an inflexible standard of care (especially with dose limitations)
- Not intended to be a law, regulation or policy that dictates clinical practice
- Focus is on initiation, patient selection, duration and follow up care
- Addresses the misapplication of the 2016 guidelines

The "Legacy" Patient

- Previous guidelines did not address
- Often high dose opioid therapy
- Long-standing opioid therapy
- Emphasizes clinician-patient decision making
- Important to establish goals
- Guidelines emphasize flexibility
  - Dose and duration are seen as flexible and not rigid standards

Contributing Factors to Opioid Reduction

- Awareness and education
- Regulatory oversight
- Fear
- Increased vigilance
- Targeting of misuse
- Better awareness of misuse and addiction
- Tightening of availability of opioids

Contributing Factors to Inadequate Management and Prescribing

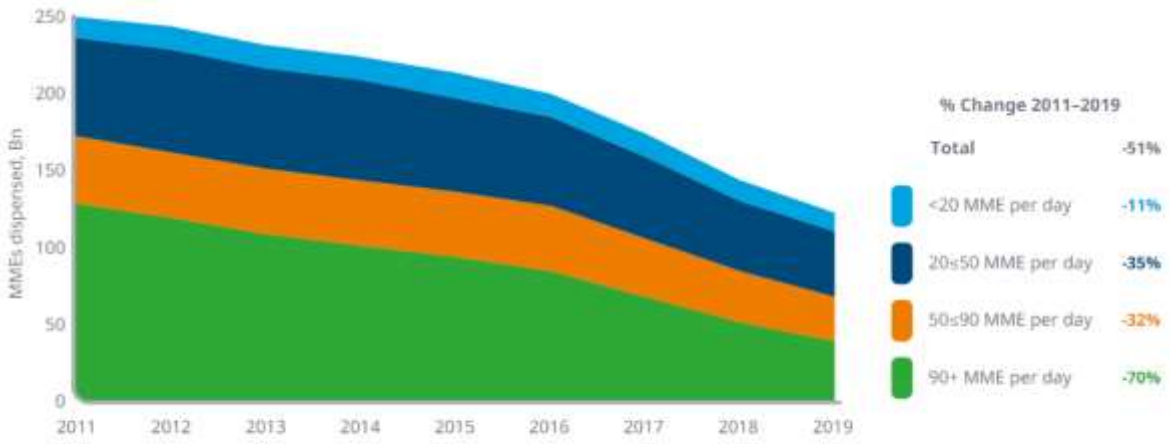
- Physician lack of knowledge in best clinical practice
- Inadequate research
- Poor understanding of risk mitigation
- Lack of multi-modal treatment
- Physician misunderstanding of dependence/addiction
- Complete relief may not be an attainable goal

Signs of Progress

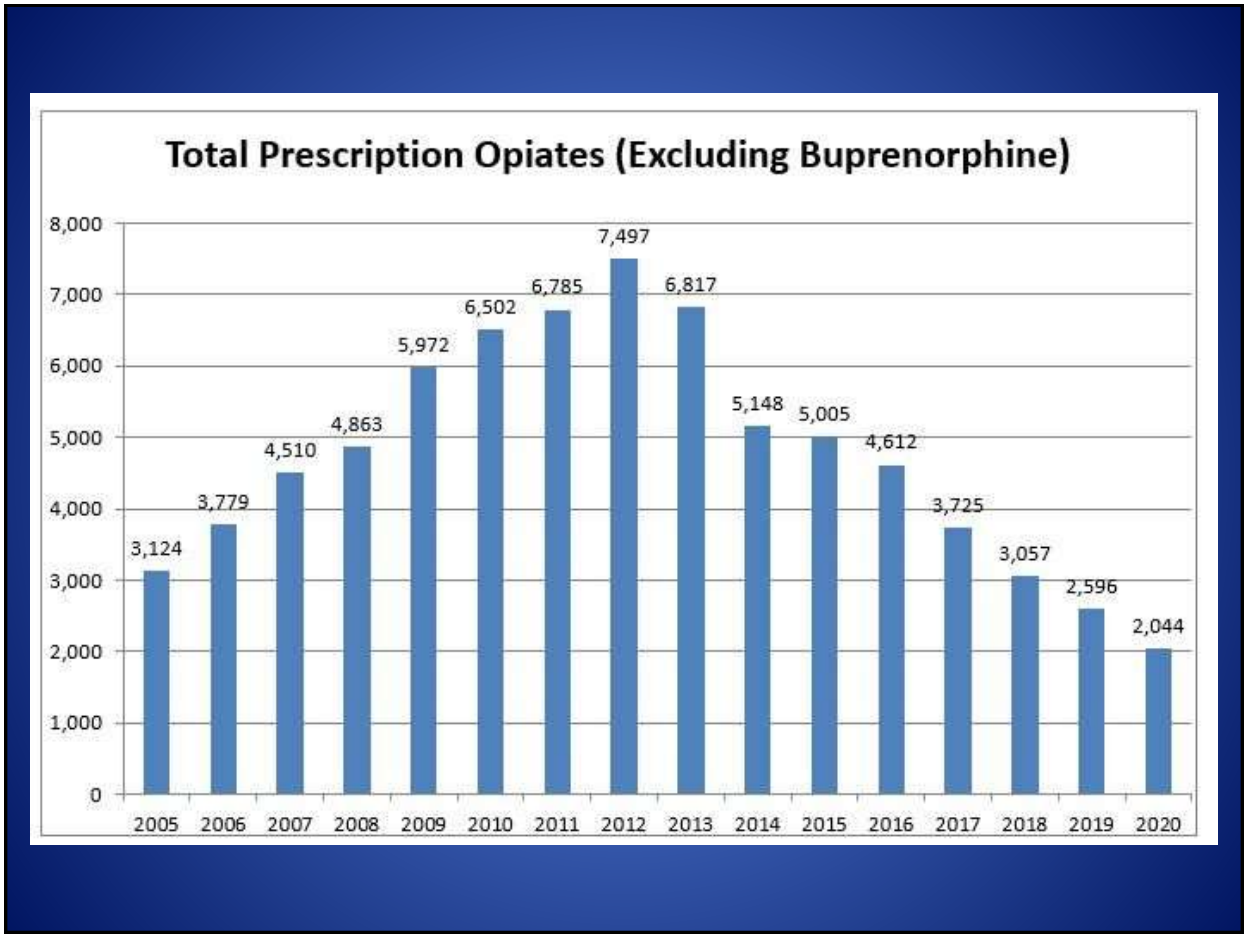
- Reduction of prescription opioid deaths
- Reduction of high MME's (< 100)
- Lessening of total opioids prescribed
- Better education and tools to assess for misuse
- Improvement in identifying and managing OUD

The greatest reduction in prescription opioid use has been in the highest risk segment, which contain more than 90 MMEs per day

Exhibit 3: Prescription Opioid Use Segmented by Morphine Milligram Equivalents (MME) per Day, 2011–2019



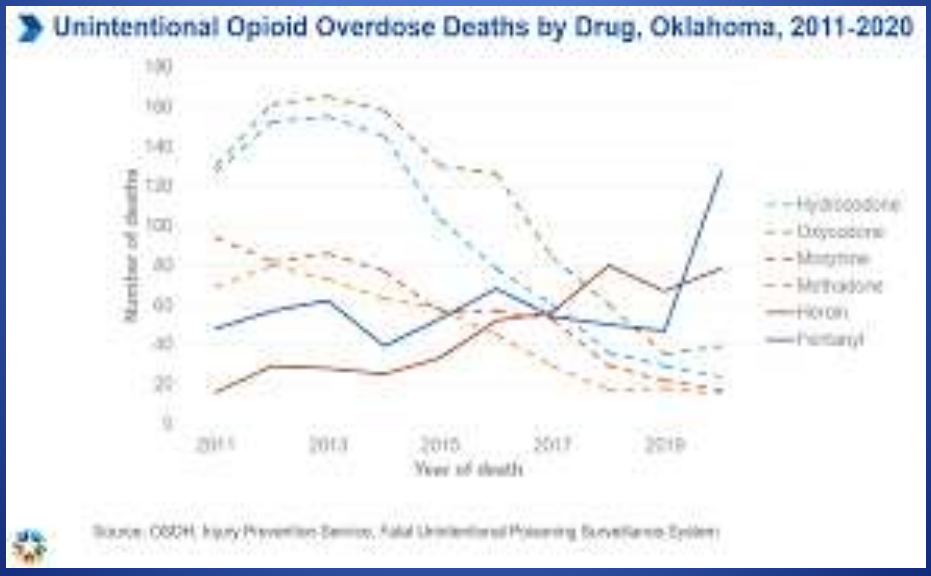
Source: IQVIA Xponent, Mar 2020; IQVIA Institute, Nov 2020


Total Prescription Opiates (Excluding Buprenorphine)
8,000
7,000
6,000
5,000
4,000
3,000
2,000
1,000
0
3,124
3,779
4,510
4,863
5,972
6,502
6,785
7,497
6,817
5,148
5,005
4,612
3,725
3,057
2,596
2,044
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020

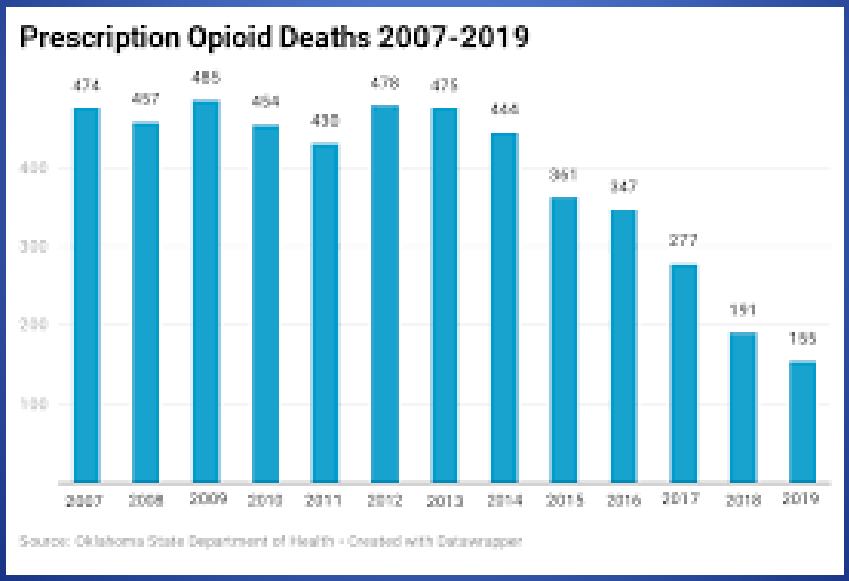
Opioid Deaths

- 108,000 deaths in US involving all opioids in 2021
- Oklahoma:
  - Methamphetamine highest overdose deaths in 2020
  - 77% of opioid deaths involved fentanyl or heroin
  - 24% increase in drug overdose deaths in 2020
  - From 2019-2020 a 170% increase in fentanyl deaths
  - Prescription opioid deaths continue to decline
  - Benzodiazepine/opioid combinations

Unintentional Opioid Deaths in Oklahoma



Oklahoma Prescription Opioid Deaths



SUDORS Data 2020: Oklahoma

- 20.8 deaths per 100,000 persons below national average of 30.6
- Missed opportunities
  - Potential bystander present 39.1%
  - Mental health diagnosis 19.8%
  - Fatal drug use witnessed 8.9%
  - Recent release from institutional setting 8.7%
  - Prior overdose 3.3%
  - Current treatment for SUD/OUD 1.5%

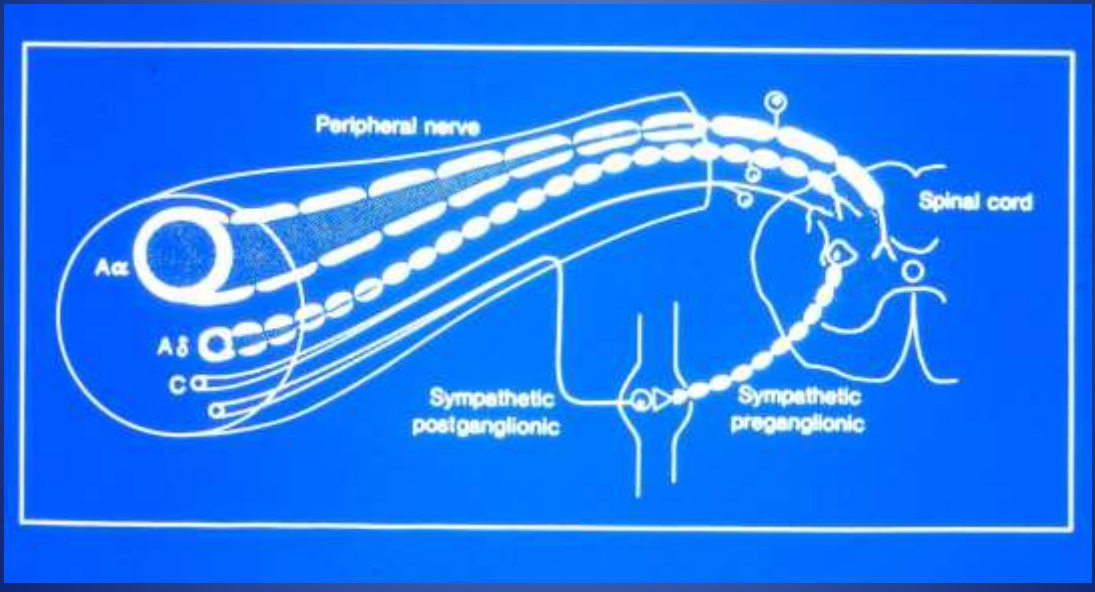
"Opioid Crisis" Confusion:

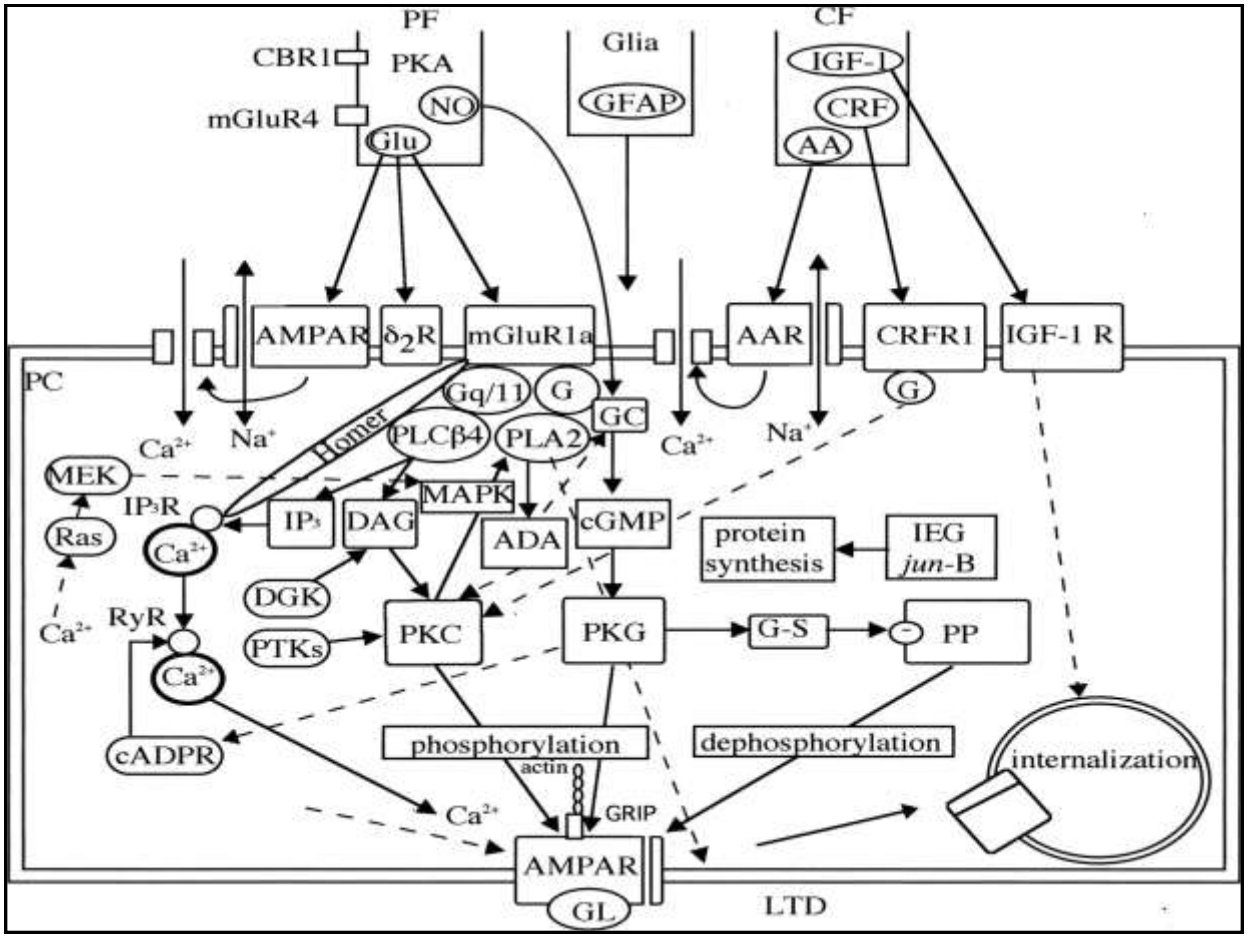
- Prescription vs. illicit opioids
- Important distinction for the chronic pain patient
- Contributes to stigma faced by patients and physicians
- A significant contributor to the reduction of opioids
- Recent AP article July 2022
  - "Opioids are claiming more lives than ever"
  - Ongoing FDA review of prescription opioids

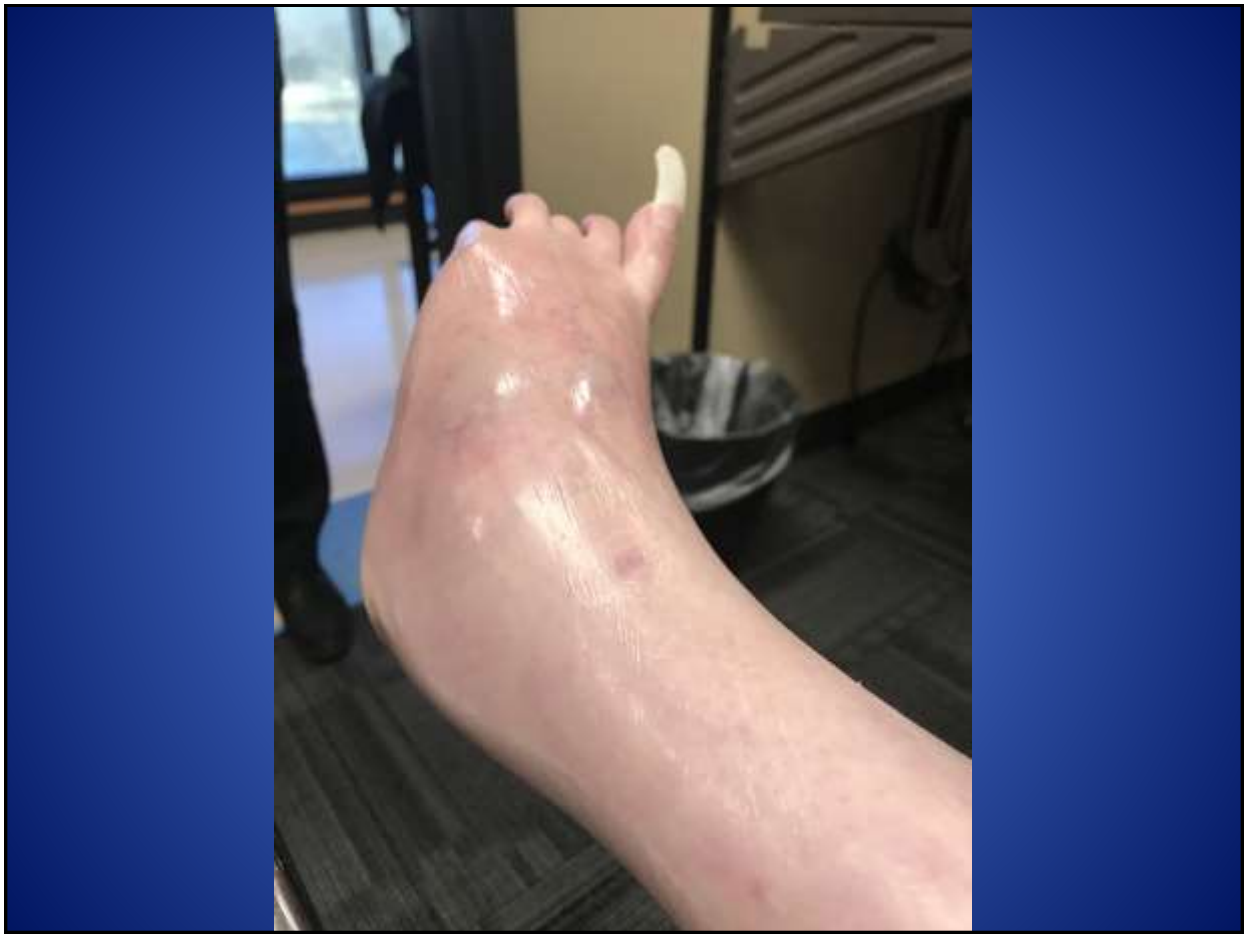
Types of Pain:

- Nociceptive pain
  - Inflammatory
  - Mechanical
  - Thermal
- Neuropathic pain
  - Hyperalgesia
  - Allodynia
- Peripheral and central sensitization

The Basic Pain Pathway

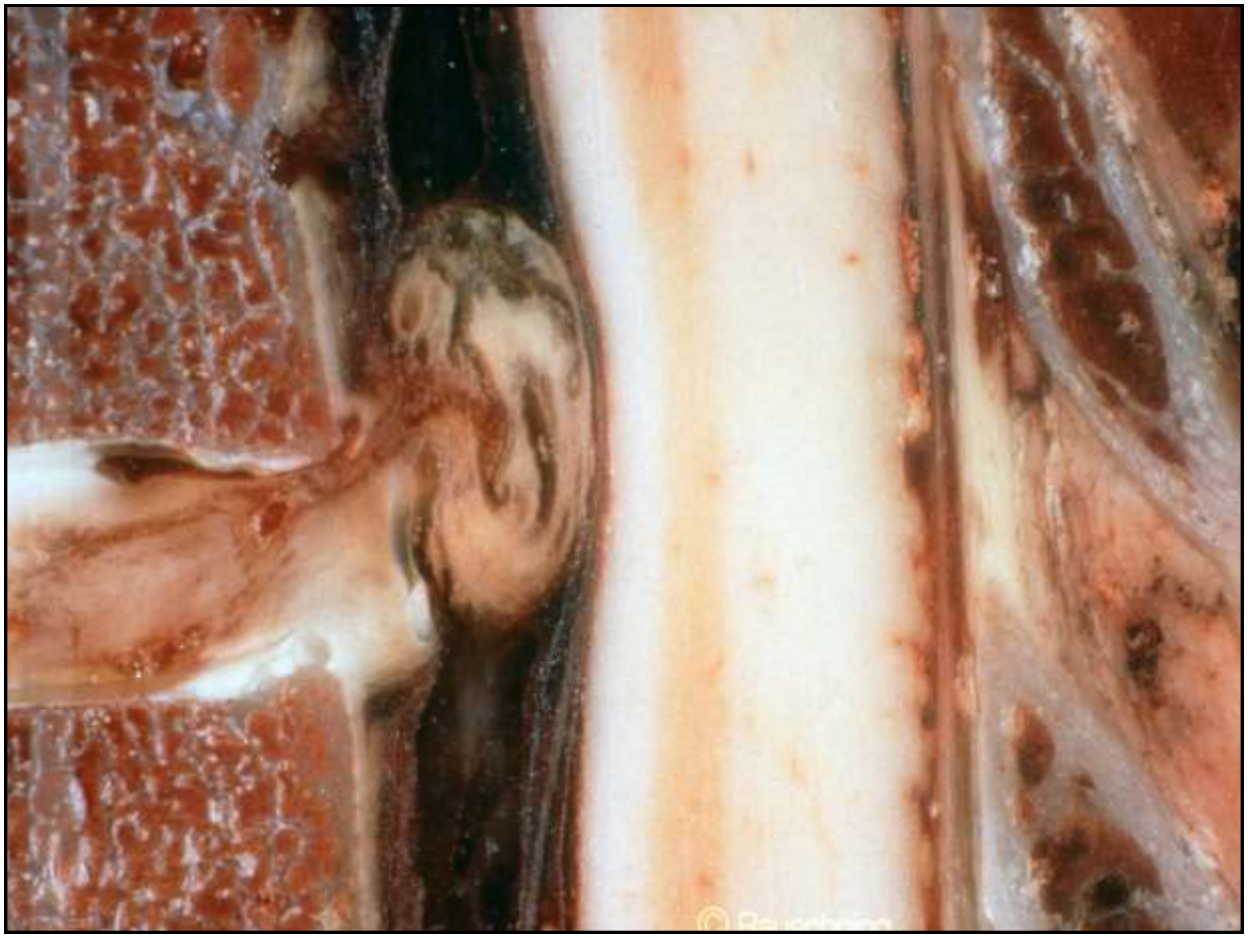


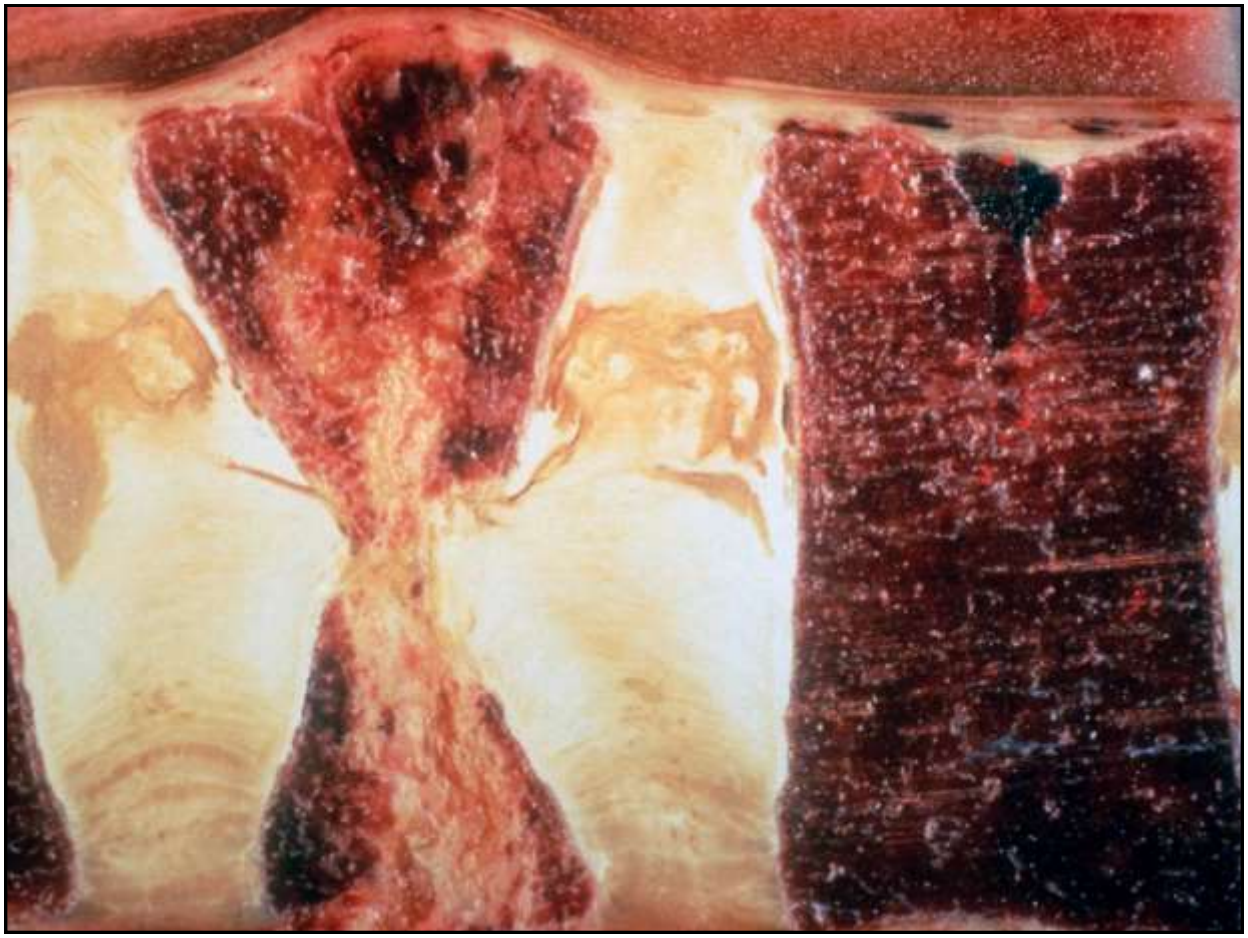

PF
CF
Glia
CBR1
PKA
mGluR4
NO
Glu
GFAP
IGF-1
CRF
AA
AMPAR
δ2R
mGluR1a
AAR
CRFR1
IGF-1 R
PC
Gq/11
G
GC
Homer
PLCβ4
PLA2
Ca2+
Na+
MEK
IP3R
MAPK
Ras
IP3
DAG
ADA
cGMP
protein synthesis
IEG jun-B
DGK
RyR
PKC
PKG
G-S
PP
PTKs
cADPR
phosphorylation
dephosphorylation
internalization
actin
GRIP
AMPAR
GL
LTD

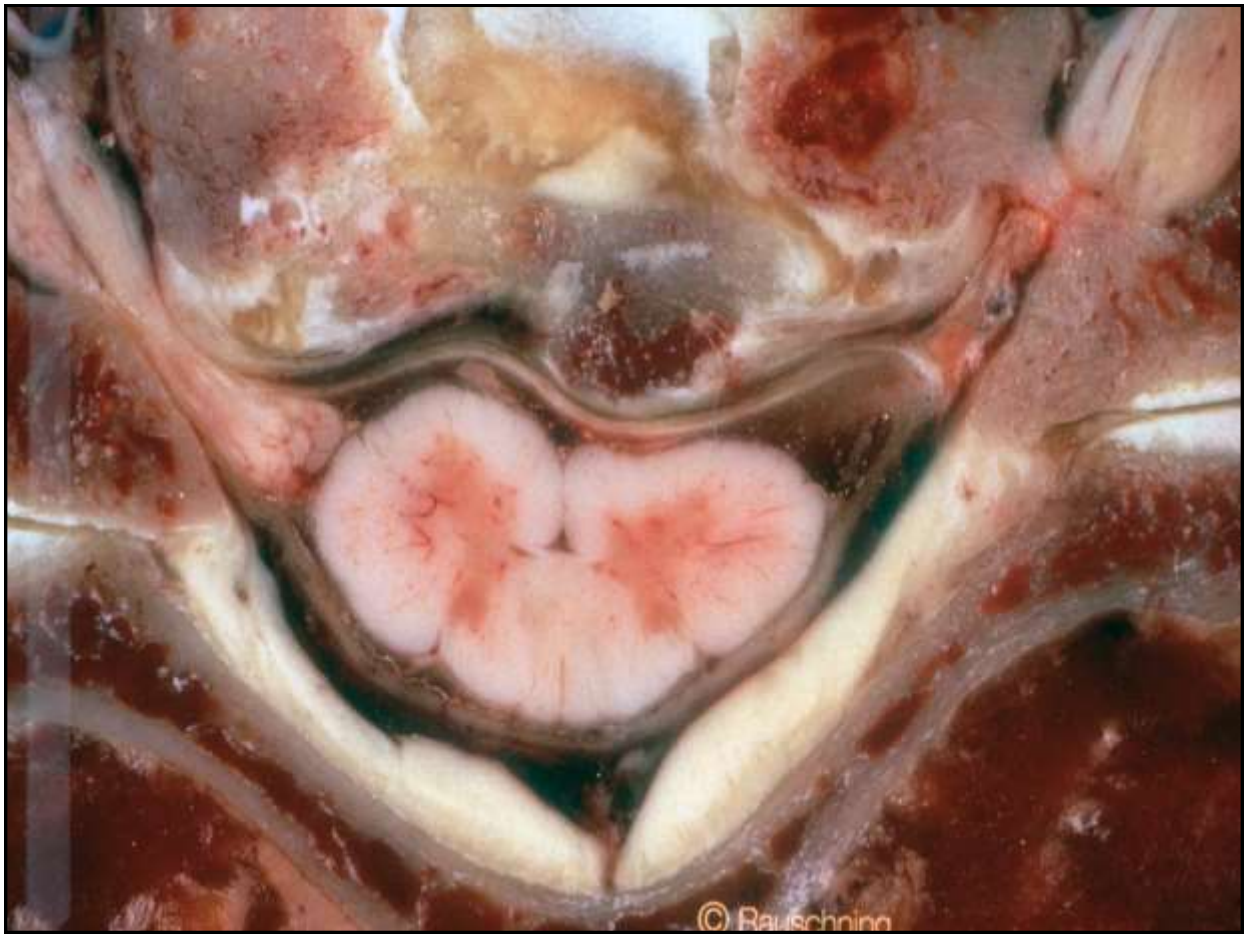


Determine a Diagnosis

- Important for determining patient selection for appropriate pain therapies
- Are other options available to the patient?
- What are we actually treating/managing?
- Not as simple as “musculoskeletal pain”



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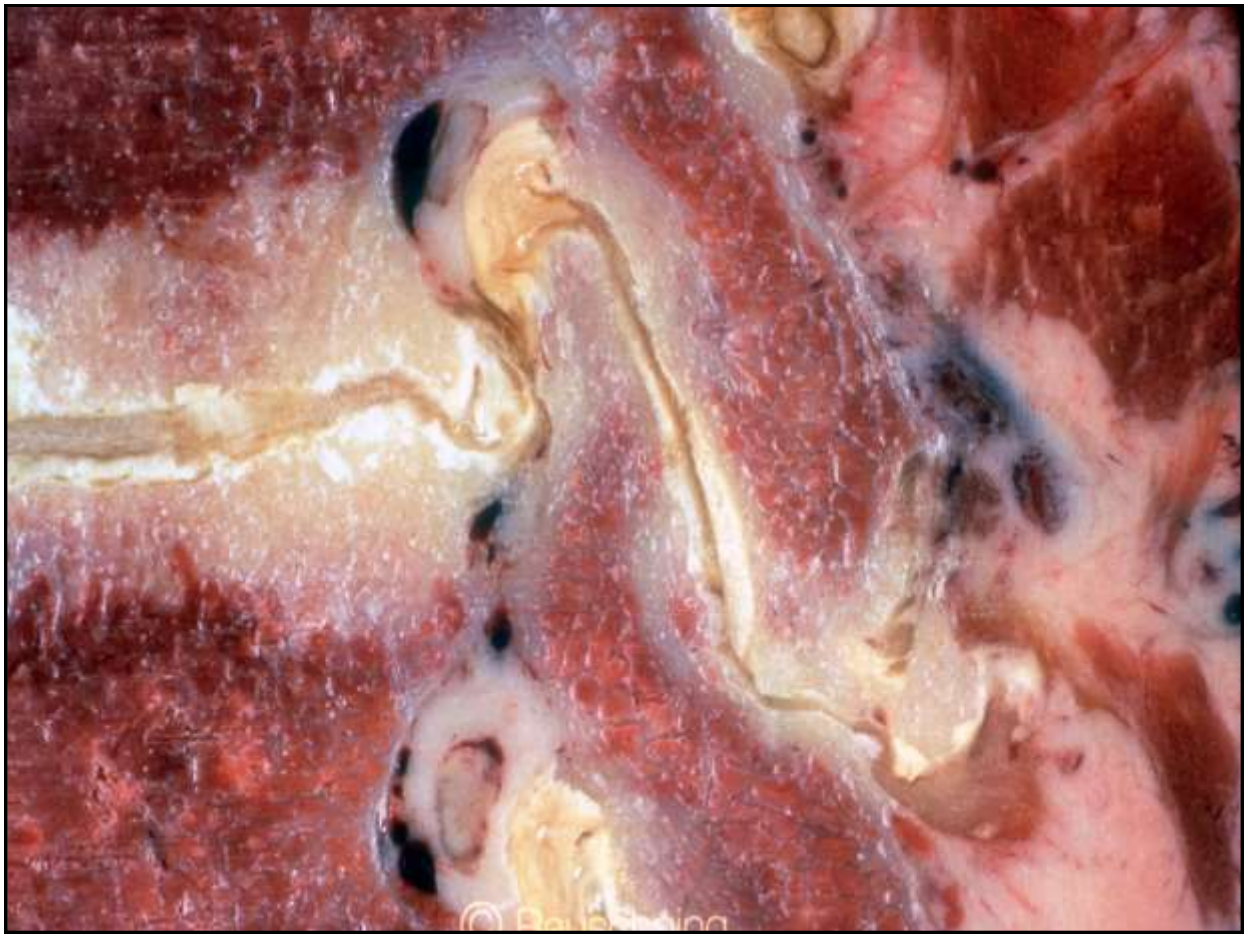


Opioids For Chronic Pain:

- Chronic pain is highly complex
- Opioids alone are often inadequate (mild-moderate)
  - 25-50% improvement in pain scales
- Opioid therapy can be beneficial in select patients who demonstrate compliance and function
- Often the only remaining option for some patients
- Best outcomes are in a multi-modal setting

Are Opioids Efficacious for Chronic Pain?

- Long term outcome studies are lacking
- Good quality data showing moderate relief in some
- Insight based on available evidence
  - Opioid use may be the most important factor impeding recovery of function
  - Opioids may not consistently and reliably relieve pain and can decrease quality of life
  - The routine use of opioids cannot be recommended
- *Appropriate only for selected patients with moderate-severe pain that significantly affects quality of life*

2022 CDC Emphasis:

- Patient selection
- Understanding different pain states
- Understanding risks of higher dose opioids
- Having an “exit plan”
- Guidelines for tapering
- Avoiding abandonment
- Awareness of OUD and misuse

First Line Approach

- Important issue in SB1446/848
- Non-pharmacological approach
- Non-opioid approach
- Emphasis on
  - Behavioral therapies
  - Functional therapies
  - Adjunctive medications
  - Interventional therapies

Patient Selection and Risk Stratification

- History, physical examination and diagnostic testing
- Psychosocial risk assessment
- Expectations: physician and patient
- Risk assessment is an underdeveloped skill for most clinicians
- SB1446/SB 848 requires vigilant monitoring for abuse and addiction
- SB1446/SB 848 emphasizes documentation of the progress of the patient to the treatment objectives

Chronic Opioid Therapy (COT)

- Consensus agreement that it can be useful in carefully selected patients with moderate to severe pain
- Absolutely demands:
  - Compliance: As with any medical problem
  - Documentation
  - Vigilant monitoring for SUD and OUD
  - Assessment of opioid related side effects
  - Understanding of opioid use in chronic pain

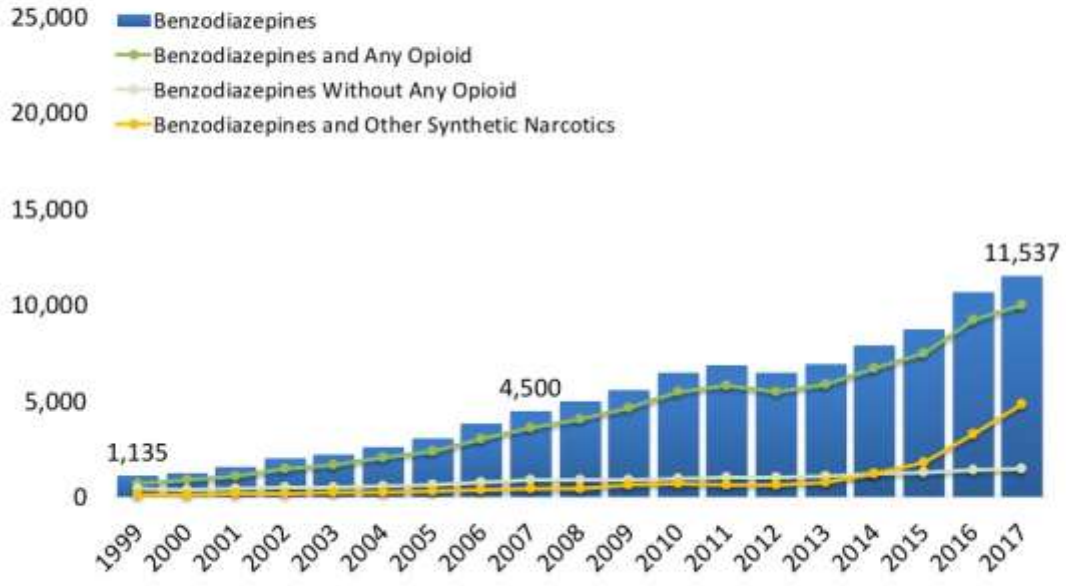
Appropriate Initiation of COT

- Informed consent and discussion of risk vs. benefit
- Therapeutic trial of 4-6 weeks with exit strategy
- Exhaustion of other modalities (within reason)
- Avoidance of ER/LA opioids
  - Start low-go slow
- Ongoing monitoring and assessment of benefit vs. risk, expectations and alternative modalities
- Consider a taper or wean even in functional patients

Opioid Prescribing Caveats:

- IR vs. ER/LA opioid therapies
- Lowest effective dose
- Benzodiazepine use with opioids
  - Significant increase in deaths and ER visits
- COPD and sleep apnea
- Combine with other modalities
- Offering naloxone to patients at risk (50 MME's)
- Ongoing assessment of psychological risks

Figure 8. **National Drug Overdose Deaths Involving Benzodiazepines, by Opioid Involvement,** Number Among All Ages, 1999-2017



Source: : Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2017 on CDC WONDER Online Database, released December, 2018

Moderate to High Dose Opioids

- Benefits are not well established but risks are higher
- Providers should prescribe lowest possible dose
- Additional precautions at > 50 MME's
- Should try to avoid > 90 MED's
- Risks of fatal and non-fatal overdoses increase
- Demands documented increase in function and no or manageable adverse side effects

High Dose Opioid Therapy

- Doses >50 MME more likely to provide diminishing returns relative to the risks
- Defined typically as >90 MME's
- Strong evidence linked with poor outcome
- Higher risk of OUD
- 9x increase in deaths with 100mg or higher MME
- Remember, existence of persisting pain does NOT constitute evidence of undertreatment

"Forced" Dose Reductions

- There is really no evidence for this approach
- A vulnerable population of patients
- Evidence shows harm
- Rupture of patient-physician relationship
- Increased disability, overdose and suicide
- Risk of illicit drug use
- An exception is severe side effects

Tapering Considerations

- Patient education and discussion of risks and benefits
- Patient agreement and interest is paramount
- Patient collaboration on plan including length of taper and perhaps a pause.
- This can take months
- Avoidance of withdrawal symptoms
- Goal may not be cessation but lower dose
- Frequent follow up
- Buprenorphine

The Fumbled Hand-off:

- ER visits and discharge
- Post op pain control
- "Pain contract"
- Discharge of a patient
- Termination of patient after failed UDS
- Transfer of a patient
- Do NOT abandon the patient. Provide for some type of "soft landing"

Characteristics of Ideal Patient

- Well defined pathology
- Good insight and desire to improve
- Willing to "work hard" to improve
- Interested in other modalities and work-up
- Not focused on opioids but desire to improve
- Good understanding that opioids will provide "some" relief to help them improve
- Examples

The Worrisome Patient

- Diffuse and poorly localized pain
- No interest in work-up or other modalities
- Focus is on opioids alone
- Poor insight and unrealistic expectations
- Poorly motivated with no desire to “work hard”
- Poor functionality
- Examples

Patients at Risk

- Psychosocial issues
- History of Substance Use Disorder (SUD)
- Adverse Childhood Experience (ACE)
  - Abuse, neglect, household dysfunction and traumatic stressors
- Poor motivation and lack of insight
- No firm cause of pain delineated
- Disability, Medicaid and prior criminal activity
- Prior overdose

Substance Use Disorder (SUD)

- "The catalyst of the opioid crisis was a denial of the addictive potential of prescription opioids"
- History of alcohol, nicotine, THC, sedatives
- SUD increases risk of developing OUD
- Screening helps identify and reduce risk
- Screening tools for SUD should be incorporated prior to and during opioid therapy
- Beware: flashing light for potential OUD

Opioid Use Disorder

- 3-26% incidence
- Significant impairment or distress
- Poor insight and social support
- Inability to reduce opioids
- Inability to control use
- Often of younger age
- Social function reduced
- Failure to fulfill work, home or school obligations
- Commonly referred to as “abuse” in the literature

Common Pathways to OUD

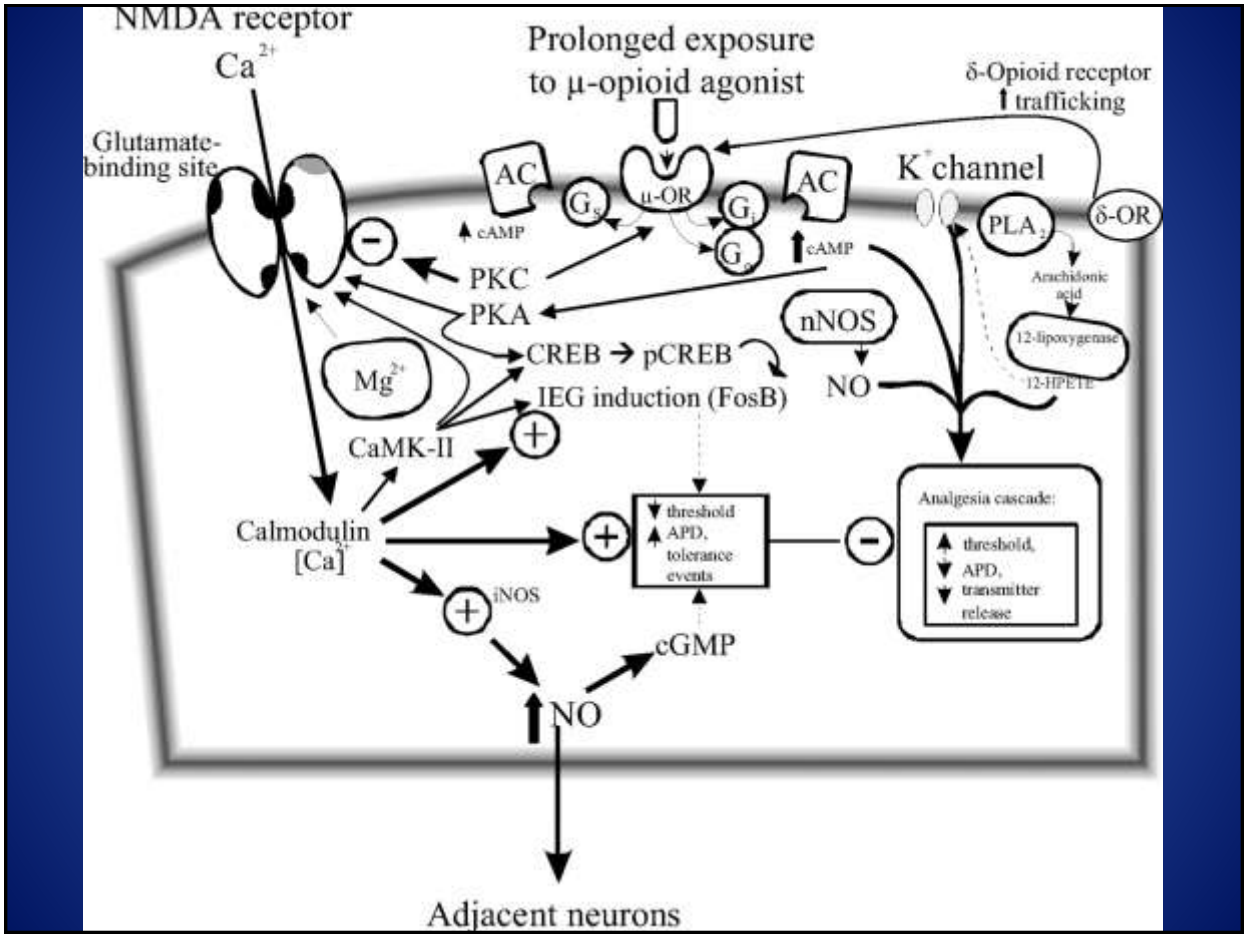
- Poor pain control (often opioids alone)
- Prior history of SUD
- Initial exposure to opioids at a younger age
- Ongoing emotional distress
- Higher opioid doses
- Long term use of opioids
- Misuse of opioids for psychoactive purposes and for unrelieved pain

Medication Assisted Treatment

- Emphasized with patients who display OUD
- Buprenorphine: Partial agonist
- Methadone
- Behavioral therapies
  - Help maintain retention
  - Help reduce relapse rate
- Consensus concerns:
  - Availability
  - Cost

Opioid Induced Hyperalgesia

- Increased sensitivity to noxious or non-noxious stimuli
- Sensitization of pro-nociceptive mechanisms
- Glial cell inflammation at the mu-receptor
- Hypersensitivity and allodynia
- Confused with tolerance
- Caused with rapid escalation and high dose therapy?
- Activity at the NMDA receptor in dorsal horn


NMDA receptor
Ca2+
Glutamate-binding site
Prolonged exposure to μ-opioid agonist
δ-Opioid receptor trafficking
AC
Gs
μ-OR
Gi
Go
AC
cAMP
cAMP
K+ channel
PLA2
δ-OR
Arachidonic acid
12-lipoxygenase
12-HPETE
PKC
PKA
nNOS
NO
CREB → pCREB
IEG induction (FosB)
Mg2+
CaMK-II
Calmodulin
[Ca2+]
threshold
APD,
tolerance
events
Analgesia cascade:
threshold,
APD,
transmitter
release
iNOS
cGMP
NO
Adjacent neurons

Common Errors

- Continued escalation of opioids despite no evidence of improvement in pain or function
- Opioids used in pain syndromes know to be poorly responsive
- Failure to document and monitor
- Not addressing psychosocial issues and OUD
- Comorbid disease states
- Utilization of sedative medications
- Rapid dose increase/decrease

Addressing Worsening Pain

- Evaluate prior to dose increase for OUD
- Common scenarios patient request for opioids or opioid increase
  - Progression of disease
  - New painful diagnosis
  - Psychological issues
  - Unrealistic expectations of pain and opioids
  - Failure to use adjunctives or other therapies
  - OUD or diversion

Risk Mitigation

- Pay attention to a pattern of activity that suggests abuse and address
- Monitor closely through follow up and documentation
- Predicting risk is challenging
- Current tools may not be very reliable
- Not a reason to dismiss patients from care

Prescription Monitoring Program

- Powerful tool
- Physician and staff friendly
- Crosses state lines
- Helpful to determine other scheduled drugs like benzodiazepines
- Good “teaching moment” with the patient
- Ideal to check before every refill
- Unfortunately a high percentage of overdoses are from non-prescribed opioids or illicit

SB1446 and 848: Major Points of Emphasis

- Addiction and abuse
- Dose reduction and cessation
- Emphasis on lower MME's
- Alternative therapies
- Strong focus decreasing the risks of acute pain leading to chronic opioid therapy
- ***Strong language for assessing, documenting and specifying your care of the opioid patient***

Prior to Issuing an Initial or Chronic Prescription

- Practitioner shall discuss and ***document*** with a note in medical record of the risks not limited to
  - Risks of addiction and overdose and risks of combining alcohol and or benzodiazepines
  - The reasons why the prescription is necessary
  - Alternative treatments that may be available
  - Risks associated with the drug being prescribed such as physical and psychological dependence, that "opioids are highly addictive" and overutilization can lead to death

Patient-Provider Agreement

- Provides informed consent
- Essentially an opioid "contract"
- Needed before the 3rd prescription and for chronic pain treatment
- Needed at initial prescription for under 18 and pregnancy
- The Boards have provided an approved agreement for use

Patient-Provider Agreement

- Explains the possible risks
- Document the understanding of patient and physician
- Establishes the rights and obligations of the patient
- Storage of opioids
- Establish specific medications and other treatments
- Specify the measures used by the physician to monitor the patient
- Delineate the process for termination of agreement
- Compliance shall constitute valid informed consent

Chronic Utilization of Opioids

- Review at a minimum every 3 months (first year) or every 6 months if compliant with PPA
  - The course of treatment
  - Any new information about the etiology of the pain
  - Progress of the patient toward treatment objectives
  - Monitor the compliance with the pain management agreement and any recommendations that the patient seek a referral
  - Check PMP (not required BUT encouraged)
  - ***Document the results***

Chronic Utilization of Opioids

- Periodically make reasonable efforts, unless clinically contraindicated, to
  - Stop use of controlled substance
  - Decrease the dosage
  - Try other medications and treatment modalities in an effort to reduce the potential for abuse or development of physical or psychological dependence
  - DOCUMENT and SPECIFY the efforts undertaken

Qualifying Opioid Therapy Patient

- ***A patient requiring opioid treatment for more than 3 months***
  - Does it matter if low dose or high dose? NO
- ***A patient who is prescribed a benzodiazepine and opioid together***
  - What about different doctors prescribing each?
  - Psychiatrist and PCP
- ***A patient prescribed a dose of opioids over 100 MME's***

References:

- Proposed 2022 CDC Guidelines. *Federal Register*, Feb 10, 2022.
- Clinical Practice Guidelines Response Draft: *Federal Register*, Feb 2022
- Oklahoma SB 1446 and SB848
- Oklahoma Opioid Overdose Fatality Review Board. Chairman's Report. January 31, 2022