CHRONIC PAIN, CHRONIC OPIOIDS: IS MY PATIENT ADDICTED?

ASAM Unit VII
Edwin Salsitz, MD, FASAM

Complex Interactions

Opioids
Pain
Addiction

Pain

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” (IASP 1994)

“Pain is whatever the experiencing person says it is, existing whenever he says it does.” (McCaffrey 1968)

“Pain is viewed as a biopsychosocial phenomenon that includes sensory, emotional, cognitive, developmental, behavioral, spiritual and cultural components.” (IASP website)
Addiction
Public Policy Statement: Definition of Addiction ASAM 2011
Short Definition of Addiction:
Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

Pain and Addiction
No Objective Measurements

Physical Dependence

"Physical dependence is the physiological adaptation of the body to the presence of an opioid. It is defined by the development of withdrawal symptoms when opioids are discontinued, when the dose is reduced abruptly or when an antagonist (e.g., naloxone) or an agonist-antagonist (e.g., pentazocine) is administered."

"Physical dependence is a normal and expected response to continuous opioid therapy. Physical dependence may occur within a few days of dosing with opioids, although it varies among patients. Physical dependence (indicated by withdrawal symptoms) does not mean that the patient is addicted."
Hedonic Tone

Sense of well being, happiness, pleasure, contentment

“Set” by/in the mesolimbic dopaminergic circuitry (Pleasure/Reward/Survival Center)

Range: Euphoria ↔ Dysphoria

Altered by Psychoactive Activities

A Delicate Balance

Human Condition

(abnormal tone in the vulnerable to addiction)
Hedonic Tone Demonstration

Opioid Dependence (DSM-IV)
(3 or more within one year)
- Tolerance
- Physical Dependence/Withdrawal
- Larger amounts/longer period than intended
- Inability to/persistent desire to cut down or control
- Increased amount of time spent in activities necessary to obtain opioids
- Social, occupational and recreational activities given up or reduced
- Opioid use is continued despite adverse consequences

Substance Use Disorder  DSM-V

<table>
<thead>
<tr>
<th>Tolerance*</th>
<th>Withdrawal*</th>
</tr>
</thead>
<tbody>
<tr>
<td>More use than intended</td>
<td>Craving for the substance</td>
</tr>
<tr>
<td>Unsuccessful efforts to cut down</td>
<td>Spends excessive time in acquisition</td>
</tr>
<tr>
<td>Activities given up because of use</td>
<td>Uses despite negative effects</td>
</tr>
<tr>
<td>Failure to fulfill major role obligations</td>
<td>Continued use despite consistent social or interpersonal problems</td>
</tr>
<tr>
<td>Recurrent use in hazardous situations</td>
<td></td>
</tr>
</tbody>
</table>

* Severity measured by number of symptoms; 0-1 mild, 2-5 moderate, 6-11 severe
* These do not apply if the medication is prescribed
Case: Robert

48 year-old male—initial evaluation 1997 Social Worker
HIV + for 15 yrs.—IVDA—1970's
F.H. +—EtOH—mother and father
Age 17-15 year-old younger brother died—leukemia 4+traumatic event for patient
Age 22 TC—Started methadone, MAT for 4 years then weaned off. No drug use since

Case: Robert, cont’d

Pain HIV neuropathy non-opioid medications not effective
Rx for Tylenol/Codeine #3—reports inadequate analgesia at 4 tabs per day
Started to take his wife's(MS) Rx 5mg Oxycodone/APAP up to 10/day
Told his MDs he was taking his wife’s opioids for ~ 1 week
Referred by HIV and PCP for opioid abuse/addiction
UDS—oxycodone, -opioids, -all else
Case: Robert

What is your diagnosis?

1. Relapsed Opioid Addiction
2. Doctor Shopping
3. Aberrant Behavior
4. Catastrophizing Pain
5. Malingering

Answer 3 is Correct

Which of the following statements are correct?

1. Opioids are contraindicated due to his previous diagnosis of opioid addiction.
2. A trial of opioid, with close monitoring, can be started.
3. If opioids are prescribed, relapse to full blown addiction is likely.
4. A patient-provider opioid agreement should be obtained.
5. Both 2 and 4 are correct.

Answer 5 is Correct

Robert: Case Summary

Rx—MS-Contin 60mg 3Xday → 60mg, 2xday after 1 year
No Problematic/Aberrant Behavior 1997—2007
All UDS neg. for non-prescribed/illicit drugs
Died July 2007—HIV/AIDS complications
### Pain and Addiction

- Chronic Pain
- OR
- Addiction
- Depression and Anxiety
- Functional Disability
- Sleep Disturbances
- Cognitive Disturbances
- Human Suffering
- Secondary Physical Problems
- Family/Social Problems
- Financial Problems

### Pain: Psychiatric Co-Morbidity

- Depression and Pain Comorbidity-Bair et al Arch Intern Med. 2003;163:2433-2445
- 56 Articles (14D>P, 42P>D)
- 65% with Depression (Dep.) have significant Pain
- ~50% in Pain Clinic have Dep.
- Pain negatively affects Dep. Outcomes
- Dep. associated with decreased pain mgmt.

### Twelve-Month Prevalence of DSM-IV Independent Mood and Anxiety Disorders Among Respondents with DSM-IV Substance Use Disorders Who Sought Treatment in the Past 12 Months

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Respondents, % (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any mood disorder</td>
<td>63.31 (5.86)</td>
</tr>
<tr>
<td>Major depression</td>
<td>14.53 (3.50)</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>23.95 (5.10)</td>
</tr>
<tr>
<td>Mania</td>
<td>20.39 (6.28)</td>
</tr>
<tr>
<td>Hypomania</td>
<td>2.46 (1.07)</td>
</tr>
<tr>
<td>Any anxiety disorder</td>
<td>42.93 (5.97)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>22.63 (5.97)</td>
</tr>
<tr>
<td>With agoraphobia</td>
<td>5.92 (2.19)</td>
</tr>
<tr>
<td>Without agoraphobia</td>
<td>8.54 (3.05)</td>
</tr>
<tr>
<td>Social phobia</td>
<td>12.38 (3.48)</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>22.52 (4.69)</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>22.07 (5.10)</td>
</tr>
<tr>
<td>Any alcohol use disorder</td>
<td>56.36 (16.40)</td>
</tr>
</tbody>
</table>

Data in parentheses are the percentages of respondents with the substance use disorders who sought treatment in the past 12 months.
Pain and Addiction-Psychiatric Co-morbidity

Association Between Mental Health Disorders, Problem Drug Use, and Regular Prescription Opioid Use

Sullivan M.D., Arch Intern Med 2006; 166:2087-2093


Odds Ratios: Major Depression—3.43  Dysthymia—6.51  Panic—5.37  GAD—2.56  Problem Drugs—3.57  Problem Alcohol—.73

Conclusion:
With initiation and use of prescribed opioids, Attention to psychiatric disorders is important when considering opioid therapy

Iatrogenic Addiction/Complex Dependence

Iatrogenic addiction occurs when a patient, [with a negative personal or family history for alcohol or drug addiction or abuse], is appropriately prescribed a controlled substance & subsequently in the therapeutic course meets the diagnostic criteria for addiction to that substance.

* There is controversy about the validity of this modifier

Opioid Treatment for Pain: Risk of Addiction

Voluminous literature including multiple systematic reviews

Rates vary widely 0%-50%—Higher in those with addiction hx

Often not clear how the diagnosis of addiction is confirmed

Aberrant and Problematic Behaviors often considered to make a diagnosis of addiction

Diagnosis is often not clear when opioids are prescribed for pain by HCP—lack of education in addictive diseases

Clinical expertise and individualization required. ASAM members uniquely qualified
Opioid Treatment for Pain: Risk of Addiction

Development of dependence following treatment with opioids for pain (Minozzi S, et al. Addiction 2012)

- Systematic review of 17 studies (N=88,235) including 3 systematic reviews, 1 RCT, and 12 observational studies

Results: Incidence = 0-24% (median 0.5%); prevalence = 0-31% (median 4.5%)

Conclusion: Opioids for chronic pain are not associated with a major risk for developing an OUD

“The most impressive finding of the present review is the deficiency of good-quality studies.”

Opioids and Pain: Risk of Addiction


- “This critique concurs with authors who have concluded that existing research is inadequate for estimating the rate of iatrogenic addiction in patients treated for non-cancer pain.”
- “Systematic reviews of many irrelevant, inadequate, and incomparable studies cannot substitute for properly designed studies”

Opioid Treatment for Pain: Risk of Addiction


Conclusions:

- The results of this evidence-based structured review indicate that COT exposure will lead to abuse/addiction in a very small % of patients. This % can be dramatically decreased by preselecting CPPs for no previous/ current hx of drug/alcohol abuse/addiction
  - 24 studies COT, 26.2 mos. (n=2,507), average % addition= 3.27%
  - 17% of studies pre-selected for no current/past hx. of addiction/abuse addition in pre-selected 0.75% vs. 5.0% in non-selected
  - Average % ADRBs =11.5%, pre-selected=0.59%
  - UDS, 5 studies n=15,642, ADRBs = 20% no opioid/other non-Rx opioid UDS, illicit drugs non-opioid = 14.5%
Systematic Review: Opioid Treatment for Chronic Back Pain: Prevalence, Efficacy, and Addiction
Martell, B. Ann Intern Med. 2007;146:116-127

Conclusion:
Opioids are commonly prescribed for chronic back pain and may be efficacious for short-term pain relief. Long-term efficacy (>16 weeks) is unclear. Substance use disorders are common in patients taking opioids for back pain, and aberrant medication-taking behaviors occur in up to 24%.

Concept of “Adverse Selection”

Opioids and Pain: Evidence Assessment

Selected Conclusions:
• Limited evidence that screening for opioid abuse using an instrument reduces abuse → Recommended
• Good Evidence that UDS reduces abuse of Rx opioids
• Good to Fair evidence that Prescription Monitoring Programs reduce drug abuse of doctor shopping
• Fair evidence that Prescription Monitoring Programs reduce ED visits, overdoses, or deaths

Treating Pain in the Addicted Patient

• “Pain Patients with a coexisting SUD are among the most challenging patients in medicine.”
• Awareness of potential deception in pt’s history
• Universal Precautions
  • “Real Pain” may make opioids less rewarding/euphorogenic
• Screening Tests: ORT, SOAPP, others
• Untreated Pain is a trigger for relapse
• Address both pain and addiction
• Significant other to secure and dispense opioid meds
• Active recovery program
• UDS, pill counts, agreements, etc.
Treating Pain in the Addicted Patient, cont'd

- UDS—consider using opioids without confusing metabolic conversions to other non-prescribed opioid analgesics: oxycodone → oxymorphone (hydromorphone, methadone)
  
  - No poppy seeds
  
  - Opioid agreement
  
  - Avoid other potentially abuseable medications: benzodiazepines, hypnotics, muscle relaxants, etc.
  
  - Identify and treat psychiatric co-morbidity—common in both

This review does not discuss the management of pain, requiring chronic opioids, in the context of active or ongoing addiction.

Methadone—FDA approved for both pain and addiction

- Addiction dosing q 24 hours
- Analgesic dosing q 6-8 hours

MMTPOs not authorized to treat pain

MMTPOs not able to provide 3-4 doses per day for pain/addiction

MMTPOs “take homes” take time

Prescribing methadone for addiction not legal—CSA

Buprenorphine pharmacotherapy formulations approved for addiction and pain. OBOT waivered physicians

Judicious use of non-opioid medications

Psychosocial modalities: MI, CBT, Acupuncture, Meditation, etc.

Pain and Addiction
Definitions: Complex Physical Dependence

Opioid Dependence vs Addiction
A Distinction Without a Difference?

"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy.
Pain and Addiction – ASAM REMS

Chronic Pain Does Not Necessarily Equal Suffering

---

Treatment of Opioid Addiction

- Medication Assisted: Therapy, Treatment, Recovery
- Opioid Full/Partial Agonist Therapy: Methadone, Buprenorphine
- Opioid Antagonist Therapy: Naltrexone Tablets and Depot I.M.
- Medication Plus Psychosocial
- Drug Free Recovery-Initially or Post-Medication

---

The Clinical Conundrum

“...as we know, there are known knowns, there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns – the ones we don’t know we don’t know.”

– Donald Rumsfeld

---
Conclusions: Known Knowns & Unknowns

- De Novo Iatrogenic addiction 0 – 50%
- Aberrant/Problematic Behaviors are common ~ 20%
- Risks are highest in those with current/past history of addiction – Multidisciplinary Team
- Monitoring patients, using Universal Precautions is helpful
- Follow the FSMBs guidelines to avoid any regulatory problems

- Is it a “Pain Case Gone Bad” or Addiction—often Grey Zone
- “Suffering is common: “Terribly Sad Life Syndrome”
- Challenging Clinical Cases—Requires Individualization Tx
- “Buprenorphine: Therapeutic Option – Pain and Addiction

*Sullivan,M JAMA Int Med 172(2012)*

**Buprenorphine: Therapeutic Option – Pain and Addiction

*Sullivan et al. Pain, 154 (2013) 1442-1448

Opioid Therapy for Chronic Pain in the United States: Promises and Perils

- 12 week studies: pain reduced 39% vs placebo
- Functional Improvement ±
- Majority of patients stop opioids: -efficacy + Aes
- COT : Less likely to return to work
- Patients with SUD or Mental Health Disorders are More likely to receive Long Term COT
- >90 days COT> long term: >120mgME> misuse
- "Adverse Selection" - The likelihood of a patient receiving COT increases as the associated risks increase

*Sullivan, Howe: Pain, 154 (2013) S94-S100

Principle of Balance

Dual obligation of governments and HCPs:

Establish system of controls to prevent abuse, misuse, & diversion of CS–opioids  Ensure medical availability