**Principles of Pain Treatment in Addiction**

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**Goals**

- Effective pain treatment
- Reduction of personal and public health consequence of opioid misuse
  - Abuse
  - Addiction
  - Diversion

**Tools**

- Physical modalities
- Biobehavioral, psychosocial interventions
- Invasive procedures
- Medications
  - Non-opioid
  - Opioid

**DEA ARCOS Data**

Reflects Opioid Therapeutic Demand

**DAWN Data**

Reflects Opioid Misuse/Harm

**TEDS data 2001**

Primary Admitting Diagnoses
Balance in Opioid Analgesia

Benefits
• Relief of pain
• Improved function
• Restoration of quality of life

Risks/unwanted effects
• Physical side effects
• Abuse or addiction
• Diversion/public health risks

Pain Treatment in Addiction Foundations

• Synergy of addiction and pain
• Identification of addiction in pain treatment
• Opioid reward considerations
• Clinical management

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Physiologic Stimulus
Nociceptive → Neuropathic

Biopsychosocial Context of the Individual

Experience of Pain

Persistent Pain

Sleep disturbance
Substance Misuse

Secondary Physical Problems
Depression
Anxiety
Increased Stresses

Functional Disability

Addiction

Sleep disturbance
Substance Misuse

Secondary Physical Problems
Depression
Anxiety
Increased Stresses

Functional Disability
Addiction Impact on Pain

- Physiologic impact of withdrawal and intoxication
  - Motor tone
  - Autonomic system
- Reinjury or strain when intoxicated
- Inability to comply with treatment recommendations
- Opioid-induced hyperalgesia

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Prevalence Addictive Disorders

- General Population: 3-18%
- Chronic Pain Population: 3.2-18%, Fishbain and Rosemoff 1992
  24% Hoffman et al 1995
- Hospitalized population: 20%
- Trauma population: 40%
- Cancer related pain: 27% (Bruera)

Prevalence Pain in Addictions

Chronic pain:
- MMT patients: 61.3% (Jamison 2000)
- 80% (Rosenblum, Joseph et al 2003)
- 37% severe
- Substance abuse treatment inpatients: 78% (Rosenblum, Joseph et al 2003)
DSM-IV Substance Dependence

1. Tolerance
2. Physical dependence/withdrawal
3. Used in greater amounts or longer than intended
4. Unsuccessful attempts to cut down or discontinue
5. Much time spent pursuing or recovering from use
6. Important activities reduced or given up
7. Continued use despite knowledge of persistent 
   physical or psychological harm

3/7 required for diagnosis
4/7 common in non-addicted pain patients

Sees and Clark, J Pain and Symptom Management 1993

Addiction

• A primary, chronic, neurobiologic disease with 
  genetic, psychosocial and environmental factors 
  influencing its development and manifestations

• Characterized by behaviors that include one or more of 
  the following:
  – Continued use despite harm (adverse Consequences)
  – Loss of Control over use or Compulsive use
  – Craving (Preoccupation with use for non-pain relief 
    purposes)

ASAM, APhA and AAPM, 2001

Use Despite Harm
(Adverse Consequences)

• Overly sedated or intoxicated with use
• Declining function due to use
  – Work
  – Relationships
  – Recreation

Loss of Control
(Compulsive Use)

• Not able to take medications as prescribed
• Reports frequent lost, stolen or destroyed 
  prescriptions
• Frequent requests for early renewals despite 
  doses determined for pain relief
• Can’t produce medications when asked
• Abusing non-prescribed drugs or alcohol
• Withdrawal signs or symptoms at clinic visits

Craving
(Preoccupation with Use)

• Does not follow other pain recommendations
• Prescriptions from multiple sources
• Preference for specific medications, especially 
  highly reinforcing medications

• A pattern of behaviors should raise concern
• Any patient using therapeutic opioids may 
  exhibit one or more of these behaviors from 
  time to time.
Patient is not likely addicted if
- Reports reasonably sustained pain control
- Demonstrates improving or stable function
- Participates in other recommended evaluations or treatments
- Discusses need for increased doses at regularly scheduled appointments
- Has no, or rare, issues with prescriptions
- Exhibits no evidence of drug or alcohol abuse

Differential Diagnosis
Addiction in Pain Treatment
- Self medication: mood, sleep, memories
- Medication of others, sharing
- Diversion for profit
  - Criminal business
  - Support medication costs
- Recreation: euphoria, rush high
- Undertreated pain

Pseudoaddiction
- Patient in pain
  - Undertreated
  - Seeks opioids to relieve pain
  - Conflicts with clinicians
  - When adequate analgesia provided, no inappropriate consequences
    - No loss of control
    - No further preoccupation
    - No adverse consequences of use

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Brain Reward Circuitry
- NA
- VTA

Weissman and Haddox, Pain Treatment in Addiction
Foundations
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Drug Reward

• Some drugs and dosing regimens induce greater reward than others
  – Rapidity of increase in blood level
  – Magnitude of blood level
  – Specific receptor effects
  – Periodicity of effects: intermittent vs stable


Opioid Reward Effects

• Do not occur in all individuals
• Pain may attenuate reward
• Opioid selection and dosing schedule may impact reward
  – Intrinsically long acting opioids
  – Controlled release opioids
  – Less rewarding opioids
  – Schedules

Drug Choice and Dosing

Reward Effects

• Intrinsically long-acting opioids
  – Methadone, levodromoran
  – Slow onset, long and variable half lives
    * More difficult to titrate for acute pain
    * Stable dose effect may increase over a week or more
  – Start low and go slow
  – Dose q 6–8 hours or longer

• Controlled release opioids
  – Morphine, oxycodone, fentanyl
  – Variable drug release profiles
  – Relatively stable blood levels
  – 12 hour dosing may reduce focus on drug taking
  – May be adulterated for rapid release
Drug Choice and Dosing

Reward Effects

- Opioids with intrinsically lesser reward
  - Partial mu agonists
    - Tramadol (dual analgesic mechanisms)
    - Buprenorphine
    - Ceiling effects
  - Agonist/antagonist medications
    - Pentazocine, butorphanol, nalbuphine
    - Kappa agonist, mu antagonist, may interfere with mu agonists
    - Ceiling effects
  - May be drugs of choice for misuse by some

- Scheduled versus intermittent
  - Scheduling avoids clock watching, negative interactions with staff
  - Pair with activity or time when possible

- Patient controlled analgesia (PCA)
  - Small increments avoid reward, dose controlled
  - Access to parenteral medications
  - Ambivalence re: self administration in some

Induction of Addiction

- Abuse cause reward through dopaminergic limbic mechanism
- Protracted/permanent changes induced in vulnerable resulting in drive to use
- Reflected in PET scans, functional MRIs
- Not all who use for reward become addicted
- Vulnerability differs among individuals
- Uncertain exposure variables: duration, dose

Etiology

- Biogenetic Predisposition
- Personal Psychology
- Addictive Disease
- Sociocultural Milieu
- Drug Exposure

Hierarchy of Endogenous Risk

Therapeutic Opioids (One View)

- Personal history opioid addiction
- Personal history non-opioid addictions
- Family history of addiction
- No personal or family history

Drug-Host Interaction

- Increasing
  - Drug Reward Potential
  - Host vulnerability
  - Lower Risk
  - Higher Risk

Stress

- Higher Risk
  - Personal history opioid addiction
  - Personal history non-opioid addictions
  - Family history of addiction
  - No personal or family history
  - Lower Risk
Spectrum of Risk
Complications of Opioid Management

Low (3/11.882*, 0/10.000**)
Remote history of addiction
Active recovery program
History of alcoholism
Short term exposure to opioids
Opioid agonist therapy

High
Active addiction
White knuckle recovery
**Longterm exposure
Non-pharmacologically assisted

*Porter and Jick, NEJM, 1980
**Heindrick

Pain Treatment in Addiction
Foundations

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Assessment of Risk
Goals

Identification of
• Risk factors
  – Personal history drug or alcohol abuse
  – Family history drug or alcohol addiction
• Abstinence or recovery
• Active addiction
• Current substance use patterns

Positive SUD History
Further Information

• Specific drugs history
• Duration of recovery
• Current recovery supports and activities
• Biopsychosocial context
• Current substance use if any

Assessment of Risk
Objective

• Physical examination
  – Signs of use: tracks, plethora etc
  – Signs of intoxication or withdrawal
  – Pathology associated with prolonged use
• Laboratory assessment
  – GGT, increased MCV (EtOH)
  – Infectious signs of IV use (HepBAg, HepCAg, HIV)
**General Principles**

Pain Treatment in Addiction

- Engage patient
- Treat pain
- Address addiction
- Address perpetuating factors and sequelae

**Engage Patient**

- Perceptions of likely treatment efficacy impacts pain experience
- Investment in plan facilitates cooperation
- Plan treatment when pain anticipated
- Self management critical to chronic pain treatment

**Treat Pain**

- Untreated pain may drive addiction, self medication and misuse
- Reduce or resolve causes when possible
- Appropriate pain relief
  - Non-medication approaches when effective, safe, easily available and acceptable to patient
  - Less-rewarding meds when safe and effective
  - Potentially rewarding meds when needed

**Address Addiction**

- Acknowledge the issues
- Assure not an obstacle to analgesia
- Encourage and support recovery

**Address Addiction**

- Address physiologic issues of drug use
  - Treat withdrawal as appropriate
  - Accommodate usual opioid doses
    - Continue methadone for OAT, add pain tx
    - Continue or rotate baseline pain opioids, add pain tx
    - Accommodate illicit opioid use, add pain tx
    - Discontinue buprenorphine, titrate opioids for pain
  - Anticipate tolerance in opioid dependent
Legal Issues

• May use any opioid, including methadone, to treat pain in any patient, including addicted patients
• Association with DEA licensed treatment facility required to use methadone and other schedule II opioids to treat addiction. Exceptions:
  – Patient hospitalized for non-addiction cause
  – Patient entering addiction treatment: 3 days, daily medications, no repeat or extension
• Buprenorphine (schedule III) is available for addiction treatment with registration/waiver
  – Currently used off-label for pain

Summary

• Addiction/pain facilitation may impede treatment and increase risk
• Effective treatment requires differentiation addiction and other challenging issues
• Opioid reward may be modulated
• Screen all patient with pain when reasonable
• Engage patient, treat pain, address addiction and other distresses

Acute Pain Treatment

Non-Opioid Addictions

• Treat withdrawal symptoms
• Provide effective pain treatment
• Non-medication, non-opioids, if effective
• Consider less reinforcing drugs, if effective
  – Scheduled, PCA, continuous infusions
  – Slower release medications
  – Agonist-antagonists, partial agonists
• Provide opportunity for recovery

Opioid Addicted Individuals

• Provide baseline opioid requirements
• Non-opioid analgesia, if effective
• Use opioids effectively when required
  – Consider tolerance in determining doses
  – Scheduled or continuous basis
  – PRN only for adjusting schedule
  – Note on-off effects short acting opioids in dependency
    PCA if continuous observation
  – Taper opioids as acute pain resolves

Acute Pain Treatment

Opioid Addicted Individuals

• Treat pain associated symptoms as indicated
• Address addiction when appropriate
  – Institute recovery activities when pain controlled
  – Stabilize or withdraw opioid when pain resolved
Acute Pain Treatment
Opioid Addicted Individuals

- Maintain control to deter medication abuse
  - Single room near nurses station
  - Limit visitors
  - Obtain consent for room searches
  - Search incoming packages
  - Frequent urine screens
  - Avoid leaving paraphernalia in room

Acute Pain Treatment
Methadone Maintained Patients

- Continue methadone po or IV (50% oral dose)
- Confirm dose with treatment program
  - If impossible, give in divided doses q 6 h
  - Or give 20-40 mg po (10-20 IV) qd maximum
- Provide additional opioid for pain control
- Use opioid other than methadone for analgesia (or not)
  - If methadone give q 6-8 h
  - Assume tolerance in dosing

Acute Pain Treatment
Buprenorphine Maintained Patients

- Buprenorphine highly avid receptor binding
  - May block mu opioid analgesia
  - May reverse mu opioid analgesia
- For acute unpredicted pain
  - Titrate higher doses of parenteral opioids
  - High intrinsic efficacy opioids eg fentanyl
- For anticipated pain
  - Discontinue buprenorphine 2-3 days before event
  - Maintain on methadone if needed

Chronic Pain Impact Inventory and Treatment Worksheet

Sensory Experience:
Sleep/Energy/Arousal:
Blood/Feelings/Thought:
Stress/Reinforcement:
Substances/Meds:
Recreation/Pleasure/Play:
Work/Creativity:
Relationships:

Opioid Therapy of Chronic Pain
Individuals with Addictive Disease

- Informed consent and written agreement
- Optimize medication schedule
  - Less reinforcing drugs when appropriate
  - Stable blood levels to avoid limbic stimulation
- Facilitate control:
  - Small scripts, clear indications for available prn, medication reviews
Opioid Therapy of Chronic Pain
Individuals with Addictive Disease

- Keys to success (*Dunbar and Katz 1996*):
  - Recovery activities
  - Social support
  - Regular appointments
  - Communication among providers and support system

Written treatment plan
- Treatment plan, specify elements
  - Addiction treatment activities
  - Monitoring of recovery
  - Medications and dosing
  - Mechanism for changing doses
  - Who prescribes, fills and dispenses
  - Management of acute exacerbations
  - Management of lost medication
  - Goals and risks of treatment

Opioid Abuse
Strategies to Minimize/Identify Early
- Provide small quantities, frequent intervals
- Dispense by trusted other
- Bring meds to clinic
- Sign and date patches, change in clinic
- Urine screens
  - Document use
  - Rule out other drugs, support recovery
- Communication between care providers
- Opioid challenge of reported dose

Assessment of Challenging Behavior
- Evaluate for behaviors suggesting addiction
  - Adverse consequences
  - Loss of control
  - Preoccupation
- If concerns
  - Refer for expert assessment
  - Modify regimen to assist in control
  - Consider urine screens for other drugs
  - Significant others may be helpful in assessing

Assessment of Challenging Behavior
- Consider inadequate dosage
  - Adjust medications as appropriate, observe
- Review for progressive or new pathology
- Evaluate for untreated sustaining factors
- Review regimen for on-off phenomena
  - Adjust medications to avoid
  - Taper if indicated
  - Manage residual pain as chronic pain
Assessment of Challenging Behavior

- Consider diversion
  - Review opioid supply at each visit
  - Consider urine screen to confirm use
  - Opioid challenge if appropriate

Opioid Definitions

- Physical dependency
- Tolerance
- Abuse
- Addiction
- Pseudoaddiction

Physical dependence

- A state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessations, rapid dose reduction, decreasing blood levels and/or administration of an antagonist

Tolerance

- A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more effects over time

Physical dependence and tolerance are not addiction

Abuse

- Use of a drug in a manner that is potentially harmful to self or others
- Use of a medication for a purpose or in a manner that is not intended by the prescriber
- From some perspectives, use of any illegal substances

Abuse is not addiction, though repeated abuse may lead to addiction in vulnerable individuals

DSM-IV Substance Dependence (Addiction)

1. Tolerance
2. Physical dependence/withdrawal
3. Used in greater amounts or longer than intended
4. Unsuccessful attempts to cut down or discontinue
5. Much time spent pursuing or recovering from use
6. Important activities reduced or given up
7. Continued use despite knowledge of persistent physical or psychological harm

3/7 required for diagnosis
4/7 common in non-addicted pain patients

Seis and Clark, J Pain and Symptom Management 1993

Adverse consequences

- Overly sedated or intoxicated with use
- Declining function due to use
  - Work
  - Relationships
  - Recreation
Loss of control

- Not able to take medications as prescribed
- Reports frequent lost, stolen or destroyed prescriptions
- Frequent requests for early renewals despite doses determined for pain relief
- Can’t produce medications when asked
- Abusing non-prescribed drugs or alcohol
- Withdrawal signs or symptoms at clinic visits

Preoccupation (Craving)

- Does not follow other pain recommendations
- Prescriptions from multiple sources
- Preference for specific medications, especially highly reinforcing medications

Pseudoaddiction

- Patient in pain
  - Undertreated
  - Seeks opioids to relieve pain
  - Conflicts with clinicians
  - When adequate analgesia provided, no inappropriate consequences
  - No loss of control
  - No further preoccupation
  - No adverse consequences of use

Opioid Reward Effects

- Multiple mu opioid sub receptors – ?? differential effects
- Rapidity/intensity of onset may effect reward
- Opioid reward effects may be attenuated by pain
- Strategies to minimize
  - Slow onset drugs (methadone, levorodromorphan)
  - Stable blood levels (continuous release/infusion meds)
  - Small increments (PCA)
  - Kappa agonists (pentazocine, butorphanol)
  - Note mu antagonism, can’t use with mu agonists
  - Partial mu agonists (tramadol, buprenorphine)
Unrelieved pain likely as great or greater risk for relapse than exposure to opioid effect.

Doverty et al., Hyperalgesic Responses in Methadone Maintained Patients, Pain V 90 (2001)
• Context: types and prevalence of drug misuse
• Etiology of abuse and addiction
• Synergy of pain and addiction
• Assessment for addiction
• Approach to pain treatment in addiction

Changes Opioid Prescribing
1997-2001

• Morphine  143%
• Hydrocodone  173%
• Fentanyl  240%
• Methadone  350%
• Oxycodone  430%
• Meperidine  -10%
Abuse

- Use of a drug in a manner that is potentially harmful to self or others
- Use of a medication for a purpose or in a manner that is not intended by the prescriber
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*Abuse is not addiction, though repeated abuse may lead to addiction in vulnerable individuals*

Physical dependence

- A state of neuroadaptation to the presence of a drug, in which a withdrawal syndrome emerges on abrupt cessation of the drug, or on rapid reduction in dose, or on administration of an antagonist

*Physical dependence is not addiction*

Tolerance

- A state of physiologic adaptation to the presence of a drug in which increasing doses of a drug are required to produce initial effects of the drug

*Tolerance is not addiction*

Opioid Induced Hyperalgesia

- Opioids may stimulate NMDA receptors
  - Hyperalgesia
  - Tolerance
  - Circumstances of occurrence poorly understood
- Methadone has NMDA receptor antagonist activity – ? clinical relevance

Cold Pressor Induced Pain

Doverty et al., Hyperalgesic Responses in Methadone-Maintained Patients, Pain V 90 (2001)

Cold Pressor Induced Pain

Doverty et al., MM Pts Cross Tolerant to the Anti-nociceptive Effects of Morphine, Pain V 93 (2001)
Substance Use Assessment

**Barriers**
- Stigmatization of drug use and addiction
- Lack of recognition of importance
- Inadequate treatment resources
- Patient resistance
- Clinician limitations

**Tools**
- Interview
- Formal Screens
- Physical Examination
- Laboratory information

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Substance Use Assessment

**Interview**
- Must be non-judgmental
- Explain importance of information
- Assume use: how often do you use?
- Estimate high quantities: do you drink about a quart (or a case) a day?
- Be aware of stages of change. Patience.

**CAGE Screen**
- Have you felt you ought to Cut down on your alcohol or drug use?
- Have people Annoyed you by criticizing your alcohol or drug use?
- Have you felt bad or Guilty about your alcohol or drug use?
- Have you had a drink or used drugs first thing in the morning to steady your nerves, treat a hangover or get the day started? (Eyeopener)
  - Positive screen: 2 of 4 positive responses
  - 85% sensitive, 90% specific


**Cyr Wartman Screen**
- Have you ever had a drinking problem?
- When was your last drink?
  - Positive screen:
    - Yes
    - Within 24 hours of medical appointment
  - 90% sensitivity

*May be asked with respect to drugs as well*

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**Sleep disturbance**
**Drug Dependence**
**Increased Stresses**
**Depression**
**Anxiety**
**Pain**
**Addiction**

**Secondary Discomforts**

Functional Disability
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*Abuse is not addiction, though repeated abuse may lead to addiction in vulnerable individuals*

Addiction

- A primary, chronic, neurobiologic disease with genetic, psychosocial and environmental factors influencing its development and manifestations

- Characterized by behaviors that include one or more of the following:
  - Continued use despite adverse consequences
  - Loss of control over use
  - Preoccupation with use for non-pain relief purposes (e.g., raving)

*Physical dependence and tolerance not necessary*

ASAM, APS, AAPM

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- Patient is not likely addicted if
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  - Demonstrates improving or stable function
  - Participates in other recommended evaluations or treatments
  - Discusses need for increased doses at regularly scheduled appointments
  - Has no, or rare, issues with prescriptions
  - Exhibits no evidence of drug or alcohol abuse
    - though diversion is possible