Principles of Pain Treatment in Addiction

Seddon R. Savage M.D.

Associate Professor of Anesthesia
Adjunct Faculty, Dartmouth Medical School

Pain Medicine Consultant
Manchester VAMC

Director,
NH ReMOTE Project

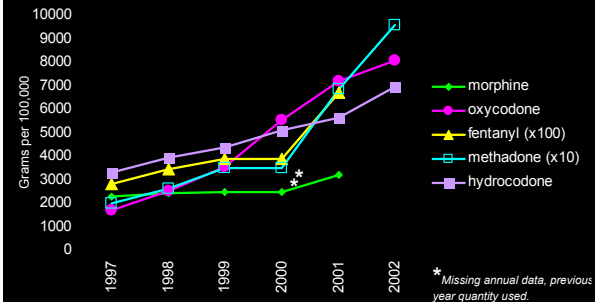
Pain Treatment in Addiction
Goals

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

Pain Treatment in Addiction
Tools

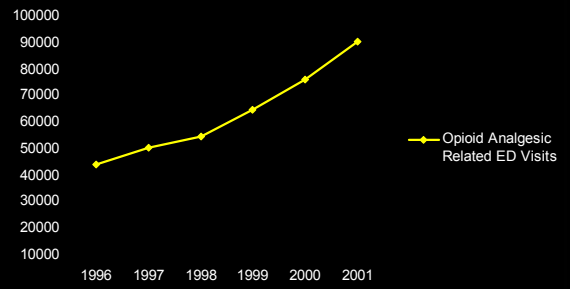
- Physical modalities
- Biobehavioral, psychosocial interventions
- Invasive procedures
- Medications
  - Non-opioid
  - Opioid

DEA ARCOS Data
Reflects Opioid Therapeutic Demand

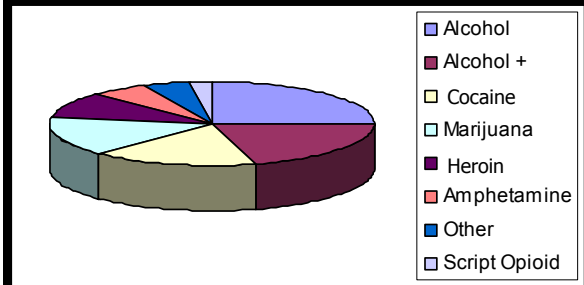


*Missing annual data, previous year quantity used.

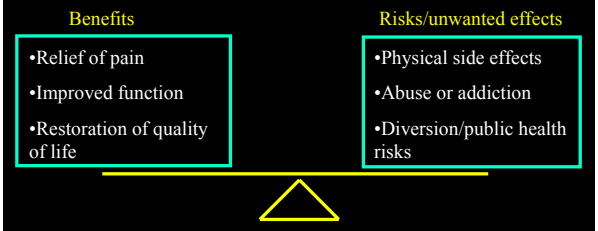
DAWN Data
Reflects Opioid Misuse/Harm



TEDS data 2001
Primary Admitting Diagnoses



Balance in Opioid Analgesia



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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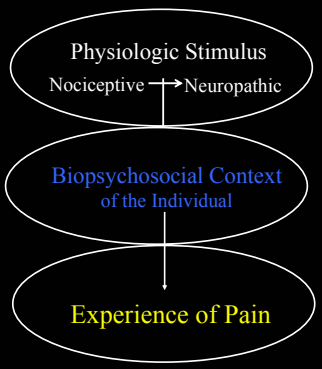

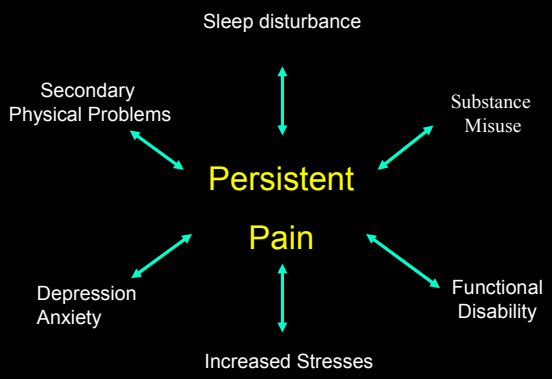

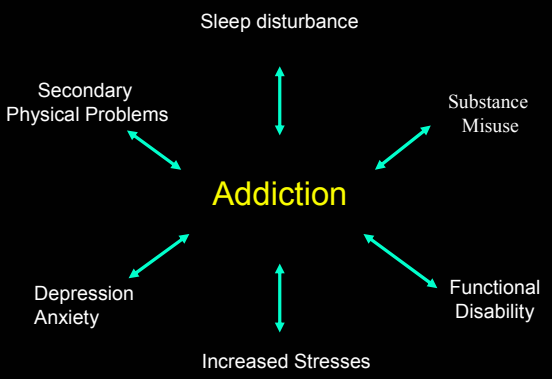

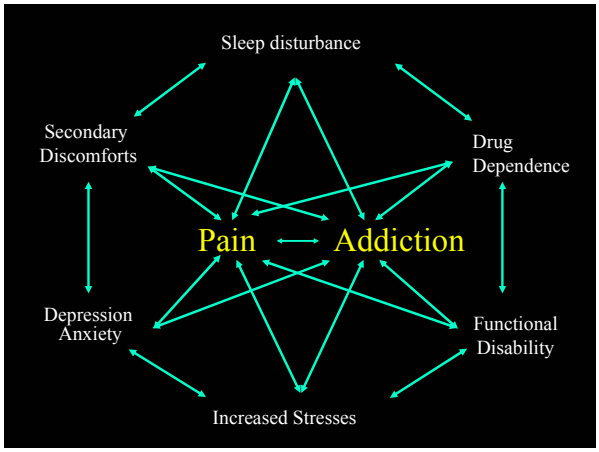

Addiction Impact on Pain

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

Pain Treatment in Addiction
Foundations

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Prevalence
Addictive Disorders

- General Population 3 18%
- Chronic Pain Population
  3.2-18%, Fishbain and Rosomoff 1992
  24% Hoffman et al 1995
- Hospitalized population 20 26%
- Trauma population 40 62%
- 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 **C**onsequences)
  - Loss of **C**ontrol over use or **C**ompulsive use
  - **C**raving (Preoccupation with use for non-pain relief purposes)

ASAM, APS and AAPM, 2001

Use Despite Harm
(Adverse **C**onsequences)

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

Loss of **C**ontrol
(**C**ompulsive 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

Weissman and Haddox,

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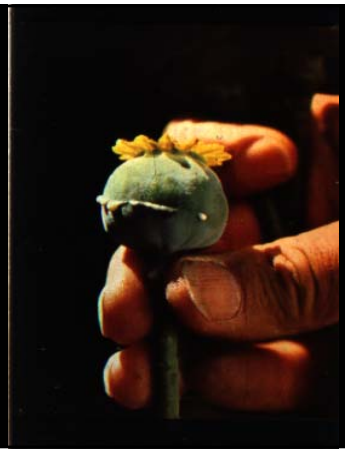
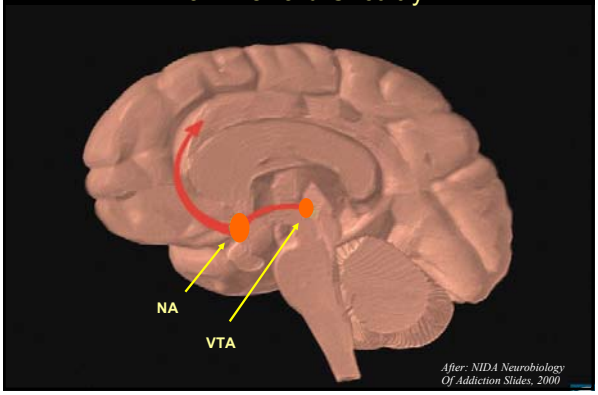


Brain Reward Circuitry



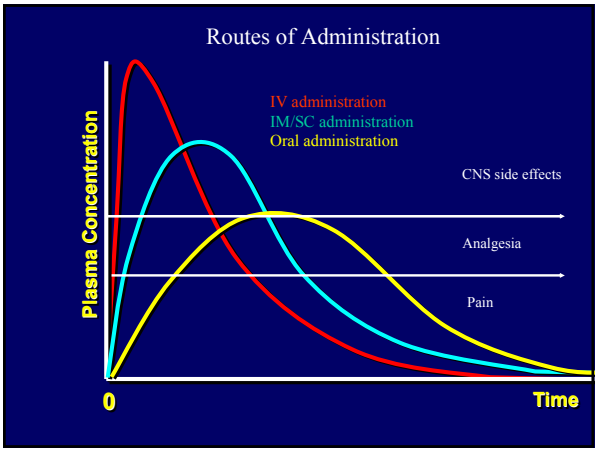
After: NIDA Neurobiology Of Addiction Slides, 2000

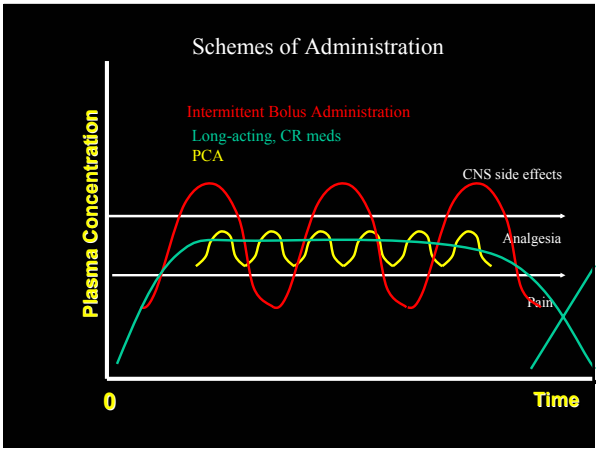
Drug Reward

- 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

MJ Kreek, Annals NYAS, 2000

Elliot Gardner, in Principles Addiction Medicine, 2003





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 8hours or longer

Drug Choice and Dosing
Reward Effects

- Controlled release opioids
  - Morphine, oxycodone, fentanyl
  - Variable drug release profiles
  - Relatively stable blood levels
  - 12 72dosing 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
    - Pentazopcine, butorphanol, nalbuphine
    - Kappa agonist, mu antagonist, may interfere with mu agonists
    - Ceiling effects
  - May be drugs of choice for misuse by some

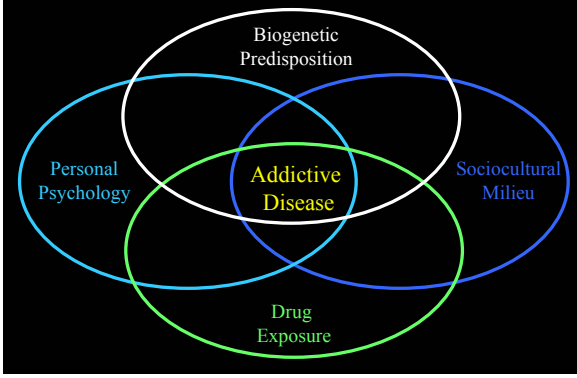
Drug Choice and Dosing
Reward Effects

- 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

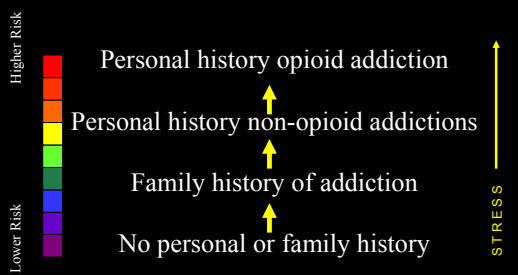
Induction of Addiction

- 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

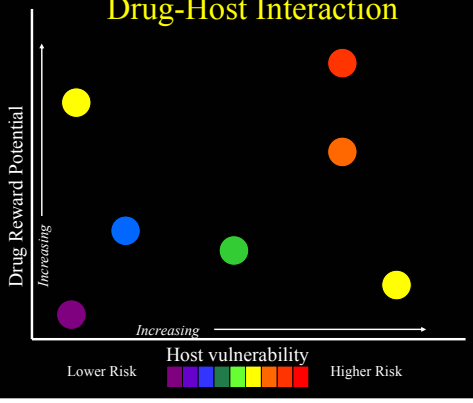
Etiology



Hierarchy of Endogenous Risk
Therapeutic Opioids (One View)



Drug-Host Interaction



Spectrum of Risk
Complications of Opioid Management

Low (3/11,882*, 0/10,000**)	(9/20***) High
Remote history of addiction	*Active addiction*
Active recovery program	*White knuckle recovery*
History of alcoholism	***History of opioid addiction
Short term exposure to opioids	**Longterm exposure
Opioid agonist therapy	*Non-pharmacologically assisted*

*Porter and Jick, NEJM, 1980
**Heindrick,
***Dunbar and Katz, J Pain & Symptom Management, 1996

After Passik, 2002

Pain Treatment in Addiction
Foundations

- Synergy of addiction and pain
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- Clinical management

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

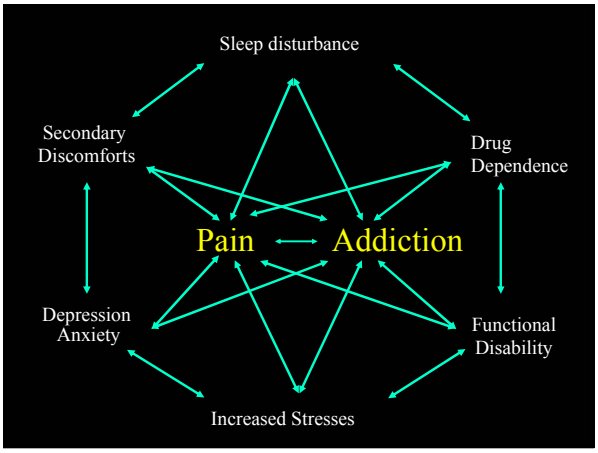
- Untreated pain may drive addiction, self medication and misuse
- Reduce or resolve causes when possible
- Appropriate pain relief
  - Non-medication approaches when effective, safe, easily available and acceptable to patient
  - Less-rewarding meds when safe and effective
  - Potentially rewarding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

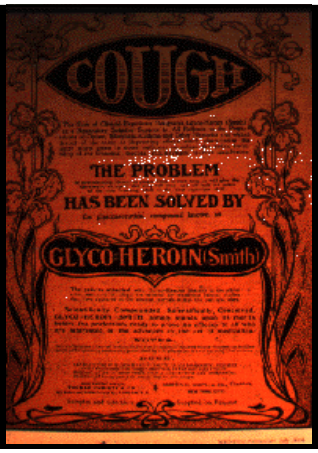


Legal Issues

- 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

Acute Pain Treatment
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 40mg po (10 20IV) 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

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 prns, 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

- 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

- 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 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

Sees 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

- A pattern of behaviors should raise concern
- Any patient using therapeutic opioids may exhibit one or more of these behaviors from time to time.

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

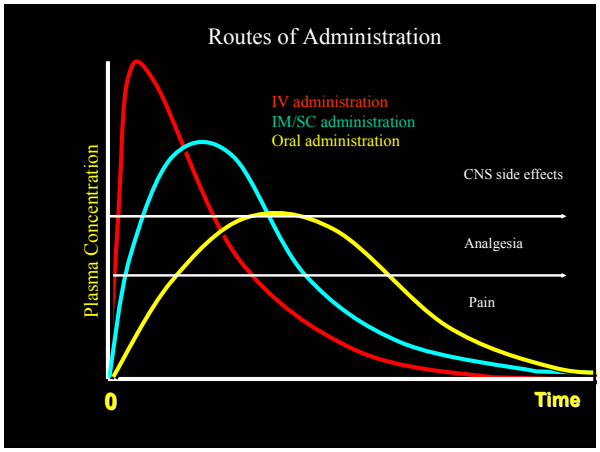
Weissman and Haddox,

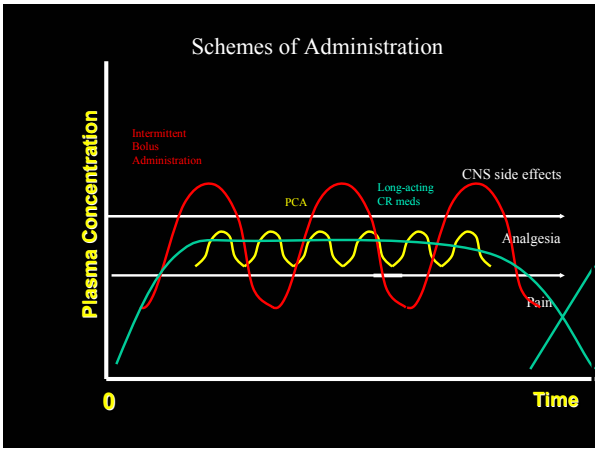
- Patient is not likely addicted if
  - Reports reasonably sustained pain control
  - Demonstrates improving or stable function
  - Participates in other recommended evaluations or treatments
  - Discusses need for increased doses at regularly scheduled appointments
  - Has no, or rare, issues with prescriptions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

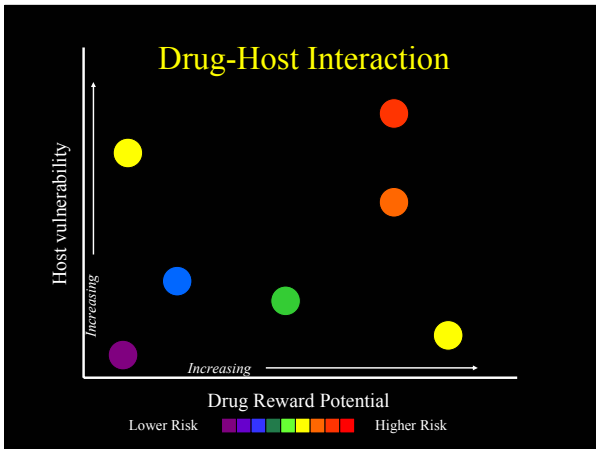
» though diversion is possible

Opioid Reward Effects

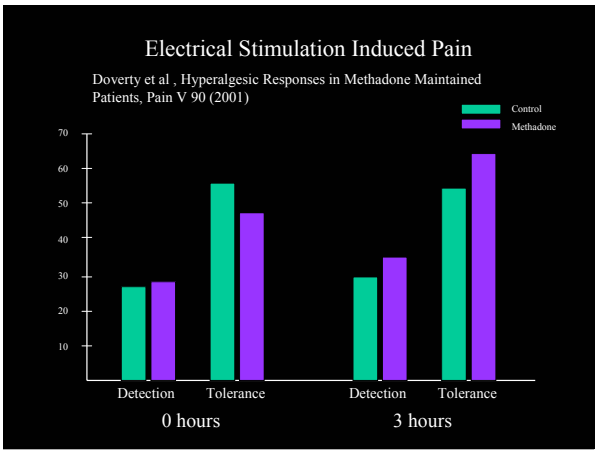
- Multiple mu opioid sub receptors – ?? differential effects
- Rapidity/intensity of onset may effect reward
- Opioid reward effects may be attenuated by pain
- Strategies to minimize
  - Slow onset drugs (methadone, levodromoran)
  - Stable blood levels (continuous release/infusion meds)
  - Small increments (PCA)
  - Kappa agonists (pentazocine, butorphanol)
    - Note mu antagonism, can't use with mu agonists
  - Partial mu agonists (tramadol, burprenorphine)





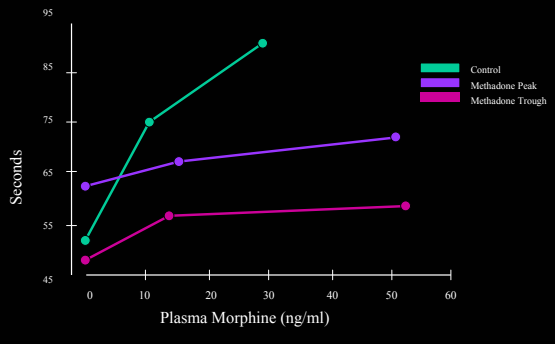


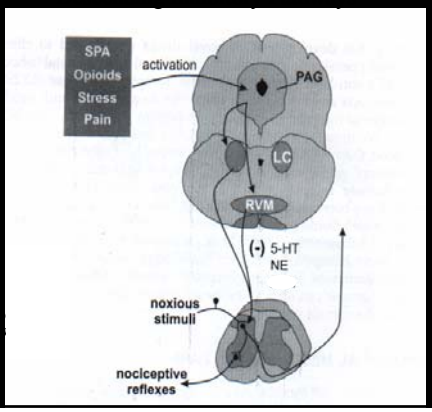
Unrelieved pain likely as great or greater risk for relapse than exposure to opioid effect



Electrical Stimulation Induced Pain

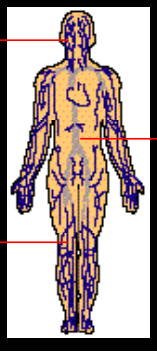
Doverty et al ,MM Pts Cross Tolerant to the Anti-nociceptive Effects of Morphine, Pain V 93 (2001)





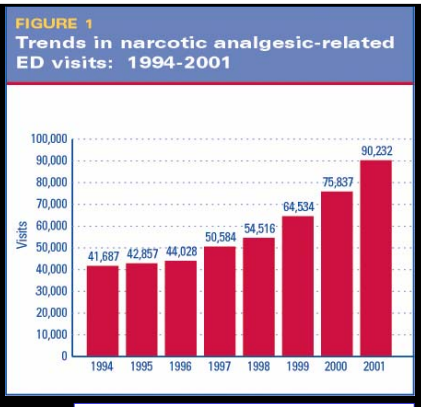
Complementary Sites and Mechanisms of Action Pain Treatments

Cognitive Therapy
Tricyclics
Anticonvulsants
Meditation
Opioids
Hypnosis

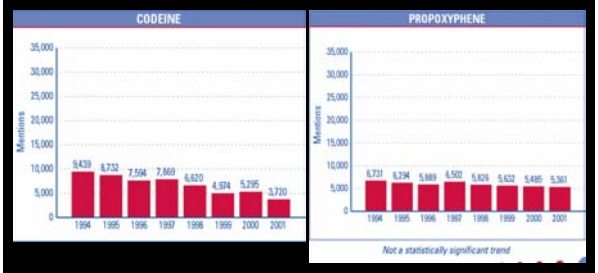


Opioids
Anticonvulsants
Sympatholytic agents
NMDA receptor antagonists
TENS
Spinal stimulation
Epidural meds
Cordotomy

Exercise
Thermal modalities
NSAIDs
Peripheral nerve blocks
Trigger point injections
Capsaicin
Biofeedback
Manipulation



Source: DAWN Report: Narcotic Analgesics, www.samhsa.gov



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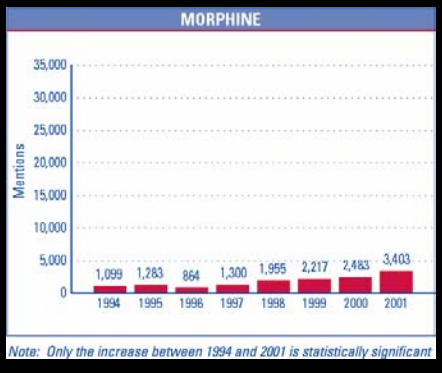

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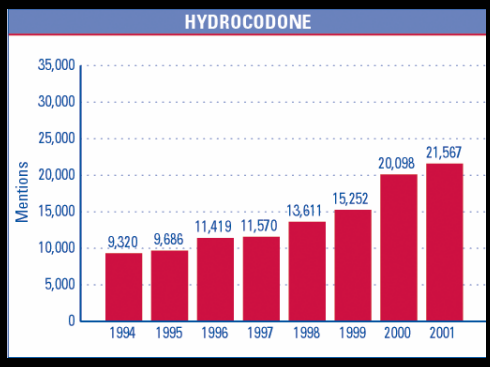
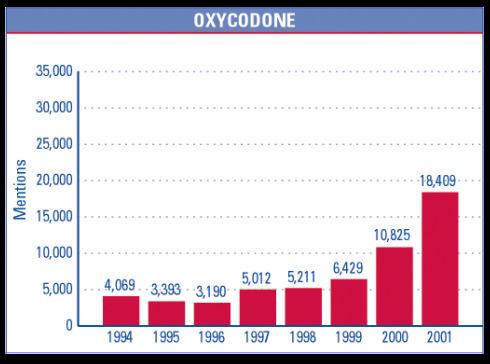
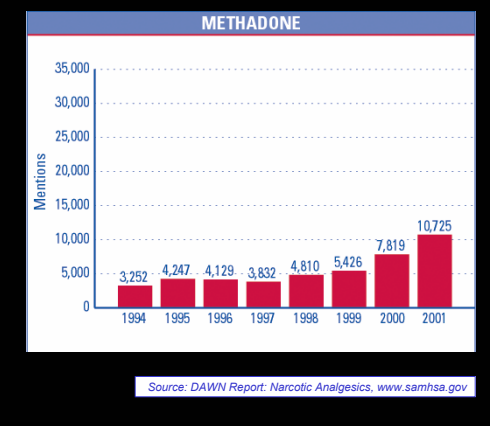
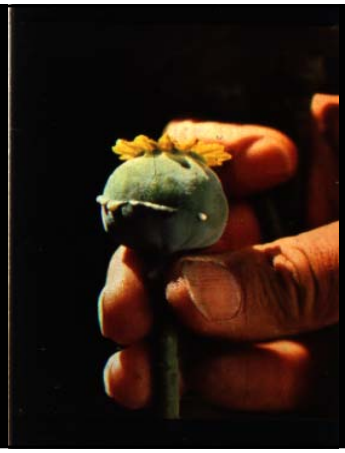






- Context: types and prevalence of drug misuse
- Etiology of abuse and addiction
- Synergy of pain and addiction
- Assessment for addiction
- Approach to pain treatment in addiction



Changes Opioid Prescribing
1997-2001

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

DEA ARCOS data

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

Physical dependence

- A state of neuroadaptation to the presence of a drug, in which a withdrawal syndrome emerges on abrupt cessation of the drug, 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

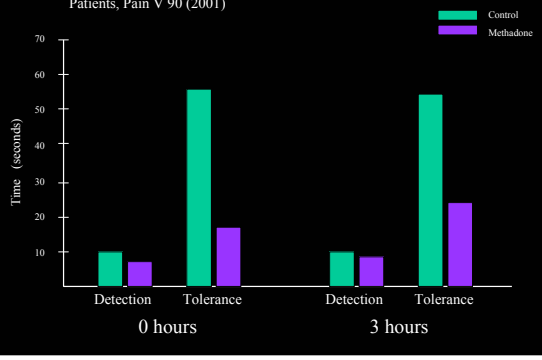
Tolerance is not addiction

Opioid Induced Hyperalgesia

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

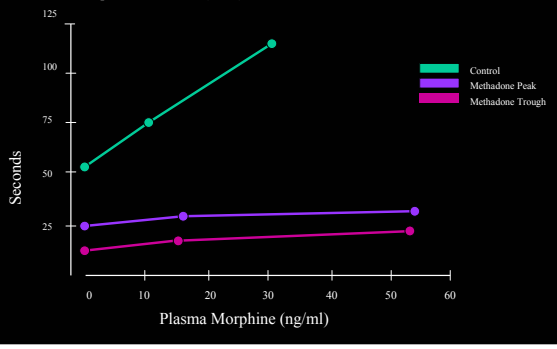
Cold Pressor Induced Pain

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

Substance Use Assessment
Tools

- Interview
- Formal Screens
- Physical Examination
- Laboratory information

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

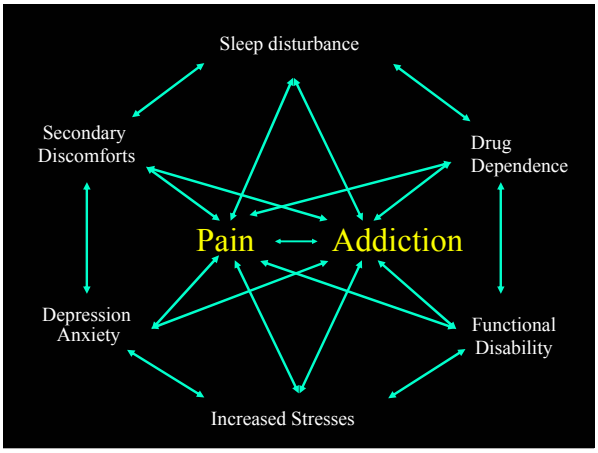
- Have you felt you ought to Cut down on your alcohol or drug use?
- Have people Annoyed you by criticizing your alcohol or drug use?
- Have you felt bad or Guilty about your alcohol or drug use?
- Have you had a drink or used drugs first thing in the morning to steady your nerves, treat a hangover or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

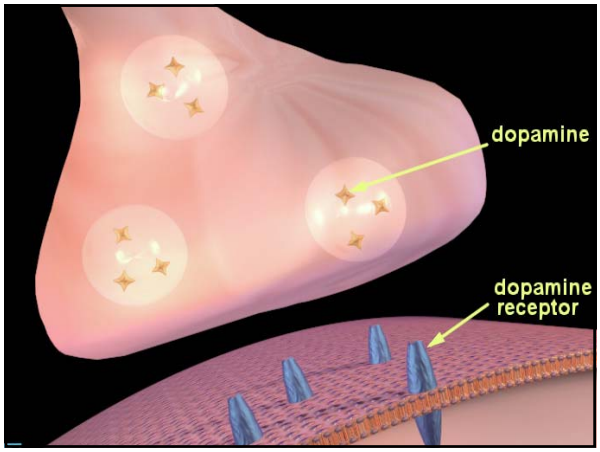
Ewiing 1984, Mayfield et al 1974, Brown and Rounds 1991

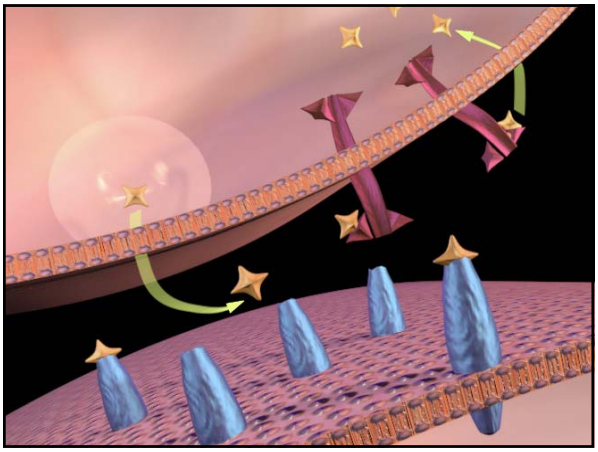
Cyr Wartman Screen

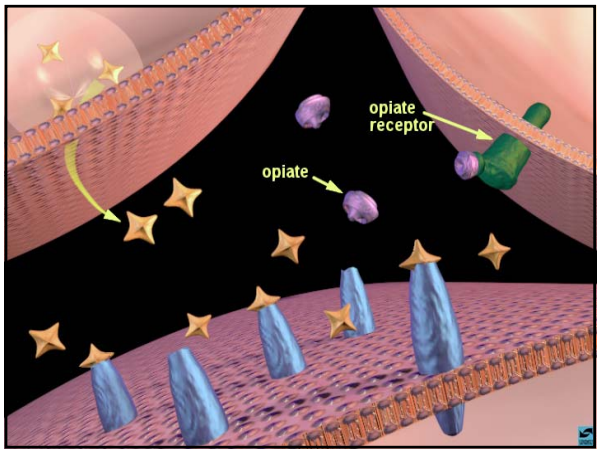
- Have you ever had a drinking problem?
- When was your last drink?
  - Positive screen:
    - Yes
    - Within 24 hours of medical appointment
  - 90% sensitivity

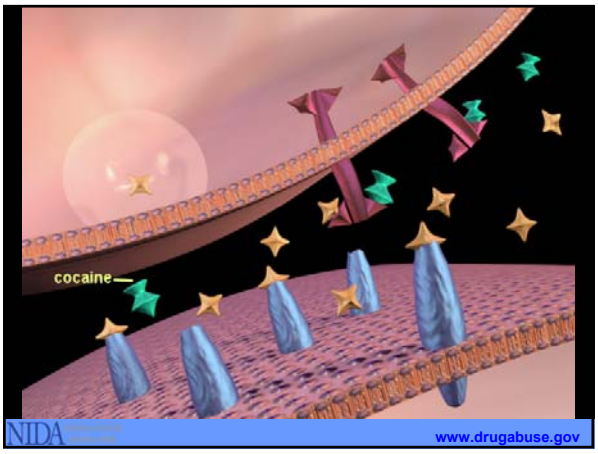
May be asked with respect to drugs as well











Opioid Definitions

- Physical dependency
- Tolerance
- Abuse
- Addiction
- Pseudoaddiction

Physical dependence

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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 (Craving)

Physical dependence and tolerance not necessary

ASAM, APS, AAPM

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

Sees 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

- 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
    - though diversion is possible

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

Weissman and Haddox,