Using methadone for opiate dependence: What counselors need to know.

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Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Savage et al., 2001
Premise of this Presentation

Drug Dependence is a brain disease with behavioral manifestations that occur in a social context.

The brain disease should be treated with pharmacotherapy.

Dysfunctional behavior should be addressed with psychosocial interventions.
Substance Dependence: A Disease With Many Interacting Causes

- Biological
- Social
- Psychological
- Genetic
- Cultural
- Environmental

Activation of the reward pathway by addictive drugs

- Alcohol
- Cocaine
- Heroin
- Nicotine
- Heroin
Pseudoaddiction

operationally defined as aberrant drug-related behaviors that make patients with chronic pain look like addicts.

these behaviors stop if opioid doses are increased and pain improves (Weissman and Haddox, 1989).

This indicates that the aberrant drug-related behaviors were actually a search for relief

Little data on the subject, but evidence in rats
Addiction is NOT:

- **Physical dependence** - characteristic withdrawal syndrome emerges upon decreased blood levels of substance or antagonist administration
- **Tolerance** - increasing amount of drug needed over time to induce the same effect

Both are *neuroadaptive states* resulting from chronic drug administration
What are opiates?

- Inducing sleep; somniferous; narcotic; hence, anodyne; causing rest, dullness, or inaction; as, the opiate rod of Hermes.
- Originally, a medicine of a thicker consistence than syrup, prepared with opium.
- Any medicine that contains opium, and has the quality of inducing sleep or repose; a narcotic.
- Anything which induces rest or inaction; that which quiets uneasiness.
Schematic of Opiate Receptor

Source: Goodman and Gillman 9th ed, p. 526
**Effect of Common Opiates at mu receptor**

- Heroin, morphine, methadone: Agonist
- Buprenorphine: Partial Agonist
- Naltrexone (Revia, Vixo)
- Nalmefene
- Naloxone: Antagonist
A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

**DSM-IV Criteria for Substance Dependence**
Physiologic Criteria:

1. **Tolerance**, as defined by either of the following:
   a) a need for markedly increased amounts of the substance to achieve intoxication or the desired effect, or
   b) markedly diminished effect with continued use of the same amount of the substance

2. **Withdrawal**, as manifested by either of the following:
   a) the characteristic withdrawal syndrome for the substance, or
   b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms
Behavioral Criteria:

3. The substance is often taken in larger amounts or over a longer period than was intended.

4. There is a persistent desire or unsuccessful efforts to cut down or control substance use.

5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
Behavioral Criteria: (Cont’d)

6. Important social, occupational, or recreational activities are given up or reduced because of substance use.

7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
Prevalence

3,744,000 persons in US reported using heroin at least once in their lifetime (2003 NSDUH)

149,000 new users (1999)

980,000 persons using heroin at least weekly (1998)

810,000 to 1,000,000 chronic users of heroin (ONDCP 2003)
Gaps in current treatment of opioid dependence

810,000 to 1,000,000 chronic users of heroin

200,000± patients receiving methadone maintenance treatment

1998 NIH Consensus Statement on Appropriate Treatment of Opiate Dependence called for increased access to pharmacotherapy.
Number of new non-medical users of therapeutics

(Number of new non-medical users of therapeutics)

(Numbers derived from NSDUH, 2002)
Commonly Abused Opioids

Diacetylmorphine (Heroin)
Hydromorphone (Dilaudid)
Oxycodone (OxyContin, Percodan, Percocet, Tylox)
Meperidine (Demerol)
Hydrocodone (Lortab, Vicodin)
Commonly Abused Opioids (continued)

Morphine (MS Contin, Oramorph)
Fentanyl (Sublimaze)
Propoxyphene (Darvon)
Methadone (Dolophine)
Codeine
Opium
Injection Drug Abuse

Photo: C. Redis
Mortality Caused by IV Drug Use  
McAnulty et al., 1995


- **Results**: 33 (1.87%) died
  - 39% OD
  - 15% trauma
  - 12% infection
  - 12% Intracranial hemorrhage
  - 9% cirrhosis

- **Interpretation**: Age-adjusted relative risk of death=8.3
Forearm

Injection Drug Abuse

Photo: C. Redis
MEDICAL COMPLICATIONS OF HEROIN ADDICTION

- FROM DIRECT DRUG EFFECT
  - Coma
  - Pulmonary Edema
  - Respiratory Arrest

- FROM UNSTERILE NEEDLE USE AND SHARING
  - AIDS
  - Hepatitis
  - Sepsis

- FROM LIFESTYLE
  - STDs
  - TB
Shoulder
Abcess postincision and drainage

Injection Drug Abuse

Photo: C. Redis
Antecubital Fossa

Injection Drug Abuse

Photo: C. Redis
Talking to patients about addiction treatment models

- Medical
- Spiritual
- Behavioral
- Psychodynamic
- Recovery
ADDICTION AS A CHRONIC ILLNESS

Chronic relapsing condition which untreated may lead to severe complications and death.
ADDICTION AS CHRONIC DISEASE: IMPLICATIONS

- It is treatable but not curable.
- Adjustment to diagnosis is part of patient’s task.
- There is a wide spectrum of severity.
- Retention in treatment is key.
- Best treatment is integrated.
Four questions patients ask:

- How is methadone better for me than heroin?
- What is the right dose of methadone for me?
- How long should I stay on methadone?
- What are the side effects of methadone?
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How is methadone better than heroin?

- Legal
- Avoids needles
- Known amount ingested
Methadone Simulated 24 Hr. Dose/Response
At steady-state in tolerant patient

“Loaded”
“High”

“Abnormal Normality”

Normal Range
“Comfort Zone”

Subjective w/d

“Sick”

Objective w/d

0 hrs. 24 hrs.

Time

Dose Response
How is methadone better than heroin?

• Legal
• Avoids needles
• Known amount ingested
• Slow onset: no “rush”
• Long acting: can maintain “comfort” or normal brain function
• Stabilized physiology, hormones, tolerance
Four questions patients ask:

• How is methadone better for me than heroin?

• What is the right dose of methadone for me?

• How long should I stay on methadone?

• What are the side effects of methadone?
What is the right dose?

- Eliminate physical withdrawal
- Eliminate ‘craving’
- Comfort/function: usually trough is 400-600 ng/ml, peak no more than twice the trough.
- Not over-sedated
- Blocking dose
Methadone Simulated 24 Hr. Dose/Response
At steady-state in tolerant patient

“Loaded”
“High”

Normal Range
“Comfort Zone”

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Subjective w/d

“Sick”

Objective w/d

trough

Dose Response

Time

0 hrs.

24 hrs.

Opioid Agonist Treatment of Addiction - Payte - 1998
Recent Heroin Use by Current Methadone Dose

Ref: J. C. Ball, November 18, 1988
Slide adapted from Tom Payte
“How Much????

Enough!!!”

Tom Payte, MD
Four questions patients ask:

• How is methadone better for me than heroin?
• What is the right dose of methadone for me?
• **How long should I stay on methadone?**
• What are the side effects of methadone?
Relapse to IV drug use after MMT
105 male patients who left treatment

Adapted from Ball & Ross - *The Effectiveness of Methadone Maintenance Treatment*, 1991
Opioid Agonist Treatment of Addiction - Payte - 1998
“How Long???
Long Enough!!”

Tom Payte, MD
Four questions patients ask:

• How is methadone better for me than heroin?
• What is the right dose of methadone for me?
• How long should I stay on methadone?
• What are the side effects of methadone?
Opiate effects, physical

Predictable physical effects of administering opiates:

- **Tolerance**: the body becomes efficient in processing the drug and requires ever higher doses to produce the desired effect.

- **Dependence**: when the drug is discontinued there are typical withdrawal signs and symptoms.
Side effects of methadone:

- General opiate effects:
  - Sedation/stimulation
  - Maintained phys. dependence (stable)
  - hypogonadism (not as severe as with heroin, may be dose dependent)

- Constipation

- Slight QTc prolongation on ECG (Martell etal)

- Sweating

- Methadone treatment tied to regulated clinic
Treatment Outcome
Data

- 4-5 fold reduction in death rate
- reduction of drug use
- reduction of criminal activity
- engagement in socially productive roles
- reduced spread of HIV
- excellent retention

(see: Joseph et al, 2000, Mt. Sinai J.Med., vol67, # 5, 6)
Crime among 491 patients before and during MMT at 6 programs

Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991
Opioid Agonist Treatment of Addiction - Payte - 1998
HIV infection rates by baseline treatment status. In treatment (IT) n=138, not in treatment (OT) n=88

Other drugs of abuse: how do they affect MMT?

- Stimulants: patients do poorly
- Alcohol: additive sedation, complicate Hep C.
- Benzodiazepines: synergistic sedation
- THC: no effect on major outcomes
- Opioids: usually blocked, tolerance
Pregnancy

- MMT treatment of choice for pregnant, opioid-abusing women.
- Efforts to avoid intra-uterine fetal withdrawal, including split dose.
- Neonatal withdrawal occurs within 72 hours, at least 45% need treatment.
- Breastfeeding recommended if not HIV positive.
Pain in patients on MMT

- Methadone is prescribed for pain treatment in twice or three times daily doses.
- Up to 60% of MMT patients have chronic pain (Jamison 2000, Rosenblum 2003)
- Split doses may be indicated.
Pharmacotherapy in context: correct glossary

- **Abstinence** includes pharmacotherapy
- **Maintenance**, not substitution or replacement (new term also: MAT)
- **Tapering from maintenance**, not detoxification, (also ‘medically supervised withdrawal’, or MSW)
- **Discontinuation**, not discharge
- **Toxicology screens**: pos/neg, not clean/dirty)
A FEW WORDS ABOUT BUPRENORPHINE

“Ceiling effect” and safety
Displaced other opiates: withdrawal on induction
Sublingual tablet
Schedule 3 (methadone is 2)
One form combined with naloxone
Office – based use available
Comparison of Activity Levels

Mu Receptor Intrinsic Activity

Full Agonist (e.g. methadone)

Partial Agonist (e.g. buprenorphine)

Antagonist (e.g. naloxone)

DRUG DOSE

no drug

low dose

high dose
Buprenorphine, Methadone, LAAM: Treatment Retention

Johnson et al, 2000
Buprenorphine, Methadone, LAAM: Opioid Urine Results

Mean % Negative

Study Week

All Subjects

Lo Meth

Bup

Hi Meth

LAAM

Lo Meth

Mean % Negative

1 3 5 7 9 11 13 15 17

19% 40% 49% 39% 19%

Study Week
Effect of counseling in buprenorphine treatment
(Fiellin, 2002)
Retention in treatment

Kakko et al, 2003,
Opioid pharmacotherapy, summary:

- Methadone, buprenorphine and LAAM all approved by the FDA for treatment of opiate dependence. (LAAM not currently available from any drug company)
- Best evidence so far supports maintenance.
- Detoxification attempts should have maintenance as a back up in case of relapse.