Treatment of the Addicted or Dependent Patient in the Family Practice Setting

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Disclosures

• Speaker and consultant for Orexo Pharmaceuticals
• Speaker and consultant for BDSI Pharmaceuticals
• Speaker for Takeda Pharmaceuticals
• Speaker for Millennium Labs
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

• 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.
Addiction is characterized by:

- Inability to consistently Abstain;
- Impairment in Behavioral control;
- Craving; or increased “hunger” for drugs or rewarding experiences;
- Diminished recognition of significant problems with one’s behaviors and interpersonal relationships; and
- A dysfunctional Emotional response.
Dependence:

• Dependence develops when the neurons adapt to the repeated drug exposure and only function normally in the presence of the drug.

• When the drug is withdrawn, several physiologic reactions occur. These can be mild (e.g., for caffeine) or even life threatening (e.g., for alcohol).

• This is known as the withdrawal syndrome. In the case of heroin, opioids, and benzodiazepines, withdrawal can be very serious and the abuser will use the drug again to avoid the withdrawal syndrome.
What addictions/dependencies do you see in your practice?
What addictions/dependencies do you see in your practice?

• Caffeine
• Nicotine (cigarettes, chewing tobacco, e-cigs)
• Alcohol
• Benzodiazepines
• Opioids
• Heroin
• Gambling
• Stimulants
• Media
• Food
• Marijuana
Nicotine

- Nicotine Anonymous
- Chantix
- Nicotine Replacement
- Behavior modification
  -- reduce one cigarette per day per week
  -- increase time between cigarettes
  -- decrease smoking environments
Alcohol

• Antabuse
• Naltrexone 50 mg pills/capsules
• Vivitrol Injectable
• Abstinence
• AA
• Specialty AA—Caduceus
• Smart Recovery (www.smartrecovery.org)
• Informal programs—Paradise Club in Akron
James and Timothy

- Partners in long term relationship
- Consuming about 7 alcoholic drinks/day
- Neither wanted to stop drinking—only reduce amount.
- Refused AA
- James—Naltrexone 50mg orally daily
- Timothy—Moderate obesity and depression treated with Contrave tapered up to full dose
- Four months later both consuming less than 2 alcoholic drinks per day and on some days totally abstain from alcohol.
Alcohol testing

Confirmatory testing

• Ethyl Glucuronide—detectible up to 80 hours
• Ethyl Sulfate—detectible up to 80 hours
• POC testing for office, but unable to obtain levels.
National Overdose Deaths
Number of Deaths from Benzodiazepines

Source: National Center for Health Statistics, CDC Wonder
Benzodiazepines

- Almost all Benzodiazepines on the street come from patients who sell their prescriptions.
- Benzodiazepines are generally used with other drugs such as alcohol, heroin, marijuana, prescription opioids, and heroin.
- Are used to bring the user down off stimulant effects—such as cocaine, LSD, or meth.
- Are used between highs, when unable to get heroin.
Benzodiazepines

• Xanax® the most popular sedative-hypnotic in terms of widespread use. (Surveillance of Drug Abuse Trends in the State of Ohio)

• Xanax® 0.25 mg sells for $0.50-$1.00
• Xanax® 0.50 mg sells for $0.50-$3.00
• Xanax® 1 mg sells for $2.00-$5.00
• Xanax® 2 mg sells for $3.00-$10.00
• Taken orally, snorted, and injected.
Benzodiazepines

- The use of most sedative, hypnotic, or anxiolytic agents can result in the development of psychological dependence, physical dependence or addiction!!
- A clinically significant withdrawal syndrome is most apt to occur after discontinuation of daily therapeutic dose (low dose) for at least 4-6 months, or with doses that exceed 2-3 times the upper limit of recommended therapeutic (high dose) for > 2-3 month.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Approx Equivalent Oral Doses, mg</th>
<th>Time to Peak Level, hours</th>
<th>Half-life, hours (max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax)</td>
<td>0.5</td>
<td>1-2</td>
<td>12</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium)</td>
<td>25</td>
<td>1-4</td>
<td>100</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.25</td>
<td>1.4</td>
<td>100</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>5</td>
<td>1-2</td>
<td>100</td>
</tr>
<tr>
<td>Flurazepam (Dalmane)</td>
<td>15</td>
<td>0.5-2</td>
<td>100</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>1</td>
<td>1-4</td>
<td>15</td>
</tr>
<tr>
<td>Oxazepam (Serax)</td>
<td>15</td>
<td>1-4</td>
<td>8</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>10</td>
<td>2-3</td>
<td>11</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>0.25</td>
<td>1-2</td>
<td>2</td>
</tr>
</tbody>
</table>

**References**
Figure 1: Illustrations of benzodiazepine metabolism.
Arrows indicate metabolic pathways.
*Norbindoxepam is also a metabolite of halazepam, medazepam, prazepam, and tetrazepam.
Why Are Metabolites Important?

- Sandra, age 37 with opioid use disorder (Suboxone 8-2 one daily)
- Severe anxiety, “jerky heart beats in throat.”
- Hands shake without Valium 15mg b.i.d. since 2013.
- Current physician has been reducing her dose.
- She “can’t function without it.”
- On disability, but won’t be able to finish her associate degree with her severe anxiety, if she is tapered from Valium.
- Sincere, straight forward, no behaviors that raises suspicion.
- Urine POC drug screen: +BUP and +BZO
Why Are Metabolites Important?

- **Confirmatory Urine Drug Screen:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cutoff ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha-Hydroxyalprazolam</strong></td>
<td>Neg 20</td>
</tr>
<tr>
<td><strong>7-Amino-Clonazepam</strong></td>
<td>Neg 20</td>
</tr>
<tr>
<td><strong>Lorazepam</strong></td>
<td>Neg 40</td>
</tr>
<tr>
<td><strong>Nordiazepam</strong></td>
<td>Neg 40</td>
</tr>
<tr>
<td><strong>Temazepam</strong></td>
<td>Neg 50</td>
</tr>
<tr>
<td><strong>Oxazepam</strong></td>
<td>Neg 40</td>
</tr>
<tr>
<td><strong>Buprenorphine</strong></td>
<td>&gt;5,000</td>
</tr>
<tr>
<td><strong>Norbuprenorphine</strong></td>
<td>Neg 20</td>
</tr>
<tr>
<td><strong>Dextromethorphan</strong></td>
<td>927</td>
</tr>
<tr>
<td><strong>Dextrorphan—metabolite</strong></td>
<td>347</td>
</tr>
</tbody>
</table>
Why Are Metabolites Important?

“Her POC urine test was positive for benzodiazepines. However, the results from confirmatory testing showed none of the expected metabolites of nordiazepam, temazepam or oxazepam. *This result is not consistent with the expected urine toxicology results from a person taking Valium (diazepam.*) In my professional opinion, there was tampering of this urine specimen. The results are consistent with the addition of Valium (diazepam) to the urine obtained from a person not taking diazepam. In my professional opinion, there was tampering of this urine specimen.
Benzodiazepines

• Assess the need for medication.
• Utilize counseling for coping with anxiety.
• Consider low dose sublingual Melatonin or Trazodone for sleep disorders.
• Be aware of addiction potential.
• Check OARRS
• Recognize the difficulty of tapering.
• Recognize the need for slow tapering.
• Death may result with sudden cessation of large amounts of Benzodiazepines.
• Be aware of potential for diversion, including family members.
Dextromethorphan

- Recreational doses:
- 100-200 mg—mild, stimulant effect (likened to MDA/Ecstasy)
- 200-500 mg—more intoxicating effect (like being ‘drunk and stoned.’)
- 500-1,000mg—mild hallucinations and mild dissociate effect (likened to low dose of ketamine) and an overall disturbance in thinking, senses and memory.
- >1,000mg—may produce a fully dissociative effect (likened to a high dose of ketamine.)
- Recreational abused doses are capable of impairing judgment, memory, language and other mental performances.
National Overdose Deaths
Number of Deaths from Prescription Opioid Pain Relievers

Source: National Center for Health Statistics, CDC Wonder
Overprescribing

• In 2010 alone, 254 million prescriptions for opioids were filled in the United States, enough for every adult in America to stay medicated around the clock for a month.

• Patients on Medicaid are prescribed painkillers at twice the rate of non-Medicaid patients, and are at six times the risk of prescription painkiller overdose.

• [Link](http://communities.washingtontimes.com/neighborhood/appalachian-chronicles/2012/jun/9/OxyContin-Bath-Salts-drug-Appalachia-addicts/#ixzz3Ol0i3i8A)
Overprescribing

• Americans (4.6% of world’s population) consume 80% of the global opioid supply and 99% of global hydrocodone supply and 66% of world’s illegal drugs.

• There has been at least a 10-fold increase in the medical use of opioid painkillers during the last 20 years.
Prescription opioids remain highly available throughout all of Ohio, except Cincinnati where street availability is moderate.

Availability has decreased in Akron-Canton, Cleveland, and Toledo over past 6 months.

Tramadol is becoming more available.

Many user’s choice of drug has switched to heroin.

Prescription opioids generally sell for $1-2 per mg.

Most common method of use is snorting, followed by oral consumption.
A profile of a typical illicit user of prescription opioids did not emerge from the data.

Typical user is “everybody.”

Prescription opioids often used with alcohol, benzodiazepines,

Cocaine and methamphetamine are used with opioid for the “speedball” effect.
Ohio Opioid/Heroin Statistics

• In Ohio, Heroin is often 10 times less expensive than pills.

• An estimated 80% of heroin addicts in Ohio started their addiction with prescription opioids.
Opioids

• Must be responsible in prescribing and document well.
• Recommend checking OARRS on every visit where an Rx is written.
• POC urine testing at every visit.
• Confirmation testing at first visit and subsequent visits as needed.
• Make certain you know for whom you are prescribing.
• Question, question, question.
• Always look at risk of addiction
• Pill counts.
• Look at alternatives for opioids.
• Use caution with NSAIDs.
Oxycodone Metabolism and Metabolites

![Diagram of oxycodone metabolism](image)

- Oxycodone is metabolized by CYP2D6 (11%) to Oxymorphone.
- Oxycodone is also metabolized by CYP3A4 (47%) to Noroxycodone.
- Oxymorphone can be glucuronosylated by UDP-glucuronosyltransferase to Oxymorphone-3-glucuronide.
- Oxymorphone can be metabolized by CYP3A4 to Noroxymorphone.
- Noroxycodone is produced from 6-keto reduction of α/β-Oxycodol (8%).
CODEINE*  
NORCODEINE  
NORMORPHINE  
HYDROCODONE* (Vicodin, Lorcet, Lortab, Norco)  
DIHYDROCODEINE  
NORHYDROCODONE  
HYDMORPHONE** (Dilaudid)  
NORHYDROMORPHONE  
NORHYDROISOMORPHONE  
MORPHINE* (Avinza, Kadian, MS Contin)  
#-Morphine  
HEROIN  
OXYCODONE (Oxycontin, Percocet, Endocet, Roxicodone)  
OXYMORPHONE* (Opana, Numorphan)  
NOROXYCODONE  
NOROXYMORPHONE  

*Forms glucuronide metabolites  
**Additionally forms glucoside metabolites
National Overdose Deaths
Number of Deaths from Heroin

Source: National Center for Health Statistics, CDC Wonder
States with the highest rate of fatal overdoses were:

1. West Virginia (35.5 deaths per 100,000)
2. New Mexico (27.3 deaths per 100,000)
3. New Hampshire (26.2 deaths per 100,000)
4. Kentucky (24.7 deaths per 100,000)
5. Ohio (24.6 deaths per 100,000)
Surveillance of Drug Abuse Trends in Ohio for Heroin June 2014-January 2015

• The current availability of heroin remains high throughout Ohio; availability has increased in six of the eight regions in past six months.

• Many participants stated heroin is now easier to obtain than marijuana and cocaine.

• Heroin is now significantly less expensive than prescription opioids.

• Some treatment providers in the Akron-Canton area noted a trend in clients using heroin without a progression from pain medication to heroin.

• Toledo participants reported that heroin dealers are so prevalent that they must deliver a high-quality product to maintain customers.
Surveillance of Drug Abuse Trends in Ohio for Heroin June 2014-January 2015

• The danger of using fentanyl-cut heroin is well understood, but most participants expressed seeking it out despite their understanding of possible overdose dangers. (China White)
• China White is also being cut with Cocaine.
• Most often noted cutting agents for heroin are caffeine, diphenhydramine, fentanyl, mannitol and quinine.
• Needles on the street sell for $1-5 each.
• Heroin costs: 1/10 gram for $20; ½ gram for $40-80; gram for $60-300 depending on quality.
Legal Stuff

• 1914 Harrison Act and the Prohibition of Addiction Treatment—illegal to prescribe opioid for the maintenance or treatment of addiction. Upheld by the U.S. Supreme Court in 1919.

  – Allows office based treatment with buprenorphine
  – Qualify physicians (8 hours of training)
  – Limit of 30 patients the first year
  – Limit of 100 patients after the first year
  – Additional DEA number beginning with an “X”
Barriers?

• They don’t need treatment, they just need to stop using.
• It’s too much work/paperwork.
• If they use heroin, they must be bad people.
• It will upset my staff.
• They don’t deserve my care.
• They are someone else’s child, sister, brother, mother, father, grandchild, aunt, uncle, cousin, friend . . . . .
Why Can’t They Just Stop? Why Do They Relapse?

- Forebrain
- Midbrain
- Dopamine Receptors
- Permanent changes in the brain
- Heroin dependence: a chronic relapsing brain disease.
Definition

Opioid Dependence: A chronic, relapsing, brain disease.
What Are Our Goals?

• Keep them alive!
• Keep them out of jail!
Rapid Detox and Taper

- 7 day taper—12% opioid free at 3 months \(\text{(Lang et al. 2009)}\)
- 28 day taper—13% opioid free at 3 months \(\text{(Lang et al. 2009)}\)
- Buprenorphine treatment—60% remain in treatment at 6 months \(\text{(2006 statistics)}\)
Medicated Assisted Treatment (MAT)

• **Buprenorphine/Naloxone**
  Suboxone 8mg/2mg  Sublingual Films
  Zubsolv 5.7mg/1.4mg  Sublingual Tablets
  Bunavail 4.2mg/0.7mg Buccal Films

• **Buprenorphine**
  Subutex 8mg Sublingual Tablets (generic)

• **Naloxone**
  Vivitrol naltrexone for extended-release injectable suspension

• **Methadone**
Where to Begin?

• Identify and understand the problem.
• It is a chronic, relapsing, brain disease.
• It is not a “character flaw.”
• We have to have the desire and compassion to help.
Where to Begin?

American Osteopathic Academy of Addiction Medicine
Telephone:  (708) 338-0760
pcssb@aoaam.org

PCSS-O is a national training and mentoring project developed in response to the prescription opioid overdose epidemic. Free. Mentoring program. pcss-o.org

American Society of Addiction Medicine
www.asam.org

http://buprenorphine.samhsa.gov (excellent resources)

Handbook of Office-Based Buprenorphine Treatment of Opioid Dependence by John A Renner Jr., M.D. and Petros Levounis, M.D., M.A.
Where to Begin?

• Step 1: Order your textbook—”Handbook of Office-Based Buprenorphine Treatment of Opioid Dependence” by John A Renner Jr., M.D. and Petros Levounis, M.D., M.A.

• Step 2: Complete your 4 hour training at home and arrange for your 4 hour face-to-face training.

• Step 3: American Osteopathic Acedemy of Addiction Medicine will help you apply for new “X” DEA Number.
Where to Begin?

• Step 4: Forms for your buprenorphine charts. [http://www.csam-asam.org/buprenorphine-info](http://www.csam-asam.org/buprenorphine-info)
• Step 5: Method to keep track of number of patients
• Step 6: Register for physician locator: [http://buprenorphine.samhsa.gov/bwns_locator](http://buprenorphine.samhsa.gov/bwns_locator)
• Step 7: Have a written protocol. (e-mail me drjamoleski@yahoo.com)
• Step 8: Determine how you will screen patients.
Where to Begin?

• Step 9: Determine your payment and fees.
• Step 10: Get your CLIA waved office drug urine/saliva tests
• Step 11: Find a lab for confirmations and metabolites.
• Step 12: Find counselors for referrals.
• Step 13: Schedule your first patient and allow a little extra time.
• Step 14: Call me if you have any questions (330-655-2668)
Rule 4731-11-12
Office Based Opioid Treatment

• Passed 01/16/2015       Effective 01/31/2015
• Non-Addiction Medicine Boarded Physicians are limited to prescribing buprenorphine 16mg or less per day.
• Mandated behavior health treatment.
• Mandatory testing for Hepatitis B, Hepatitis C, pregnancy, alcohol and toxicology testing.
• OARRS review at least every 90 days.
• Patient is limited to no more than a 30 day supply during the first 12 months.
Rule 4731-11-12
Office Based Opioid Treatment

• Eight hours of Category 1 continuing education relating to substance abuse and addiction every two years.

• Practice in accordance with an acceptable treatment protocol—any of the following:

  1. “Clinical Guidelines For the Use of Buprenorphine in the Treatment of Opioid Addiction.” (http://samhsa.gov/)

  2. “Low dose protocol approved by the Ohio Department of Alcohol and Drug Addiction Services” (http://mha.ohio.gov/)

  3. Any protocol for OBOT approved by the Ohio Department of Mental Health and Addiction Services (http://mha.ohio.gov.)
Rewards

- Save lives
- Save families
- Reduce prison population
- Satisfaction of helping patients who want help
- Protect future generation
- Financial
- Gratitude of your patients, their families, and their friends