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NIH Consensus on Drug Treatment

• Drug addiction is a disorder of the brain and therefore a medical disorder
• Broader access to drug treatment
• Reduce federal and state barriers impeding access to treatment
• Stressed the importance of providing substance abuse counseling, psychosocial therapies, and other supportive services
• Just as medication can help with depression, medication can help in the treatment of alcohol dependence, opioid dependence, cocaine dependence, nicotine dependence, etc.
If the societal cost is so high, why do people do drugs?
Addiction

• A state in which an organism engages in compulsive behavior
  – The behavior is reinforcing (that is, pleasurable or rewarding)
  – There is a loss of control in limiting the intake of the substance
Why Do People Take Drugs in The First Place?

To feel good
To have novel: feelings sensations experiences AND to share them

To feel better
To lessen: anxiety worries fears depression hopelessness
Why do some people become addicted while others do not?
Biology/genes

Biology/Environment Interactions

Environment
DA Receptors and the Response to Methylphenidate (MP)

As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant.

Adapted from Volkow et al., Am. J. Psychiatry, 1999.
Dopamine D2 Receptors are Lower in Addiction

Control  Addicted

Cocaine  Cocaine  Cocaine  Cocaine

Meth  Meth  Meth  Meth

Alcohol  Alcohol  Alcohol  Alcohol

Heroin  Heroin  Heroin  Heroin

Reward Circuits

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

Reward Circuits

Drug Abuser

Non-Drug Abuser

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

DA DA DA DA

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DA DA DA DA
Drugs Are Usurping Brain Circuits and Motivational Priorities
This is why addicts can’t just quit

This is why treatment is essential
Treatment for Addiction Includes:

1. Pharmacological (medications)
2. Behavioral Therapies
3. Medical treatment for the complications of addiction (e.g., HIV, HCV therapy)
4. Social Services
Pharmacology in Primary Care: Opioids = Buprenorphine
Heroin

- Heroin is a short-acting, semisynthetic opioid produced from opium that can be smoked, sniffed, or injected.

- Heroin euphoria begins shortly after injection and lasts ~ 1 hour, followed by 1-4 hours of sedation; withdrawal symptoms or craving begin several hours later.

- Most heroin dependent individuals inject 2-4 times per day. Many mediate sedating effects by injecting a small amount of cocaine, if available (not in Russia or Asia), known as a "speedball." Sometimes crack is smoked as a substitute.

- Unsterile use, unpredictable concentrations in street samples, adulterants in injection mixture, lifestyle necessary to procure drugs are responsible for most heroin-associated medical complications.
<table>
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<th>Binding Potential (Bmax/Kd)</th>
<th>MRI</th>
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<tr>
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<td>Bup 00 mg</td>
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<td>Bup 02 mg</td>
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<td>Bup 32 mg</td>
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Effects of Buprenorphine Dose on μ-Opioid Receptor Availability in a Representative Subject

Slide Courtesy of Laura McNicholas, MD, PhD
Medication Assisted Treatment - Opioids

- **Rationale**
  - Cross-tolerance
    - prevent withdrawal
    - relieve craving for opioids
  - Narcotic blockade
    - block or attenuate euphoric effect of exogenous opioids

- **Pharmacotherapy**
  - Buprenorphine
  - Methadone
  - LAAM
  - Naltrexone
Intrinsic Activity

Log Dose of Opioid

-10 -9 -8 -7 -6 -5 -4 0 10 20 30 40 50 60 70 80 90 100

Intrinsic Activity

Full Agonist (Methadone)

Partial Agonist (Buprenorphine)

Antagonist (Naltrexone)
Buprenorphine, Methadone, LAAM: Treatment Retention

Percent Retained

Study Week

- 73% Hi Meth
- 58% Bup
- 53% LAAM
- 20% Lo Meth
### Buprenorphine, Methadone, LAAM: Opioid Urine Results

#### Mean % Negative

<table>
<thead>
<tr>
<th>Study Week</th>
<th>All Subjects</th>
<th>Lo Meth</th>
<th>Bup</th>
<th>Hi Meth</th>
<th>LAAM</th>
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- 19% for Lo Meth
- 39% for All Subjects
- 40% for Hi Meth
- 49% for Bup
- 49% for LAAM
Buprenorphine

• Every physician treating HIV-infected drug users should have an X waiver and be ready to prescribe.

• The 1, 2, 3 of BUP:
  1. It is easier than HIV/HCV treatment.
  2. It is safer than prescribing oxycodone for pain or alprazolam for anxiety.
  3. It is desperately needed to expand access to treatment.
Pharmacology in Primary Care: Cocaine = Disulfiram
Cocaine

- Cocaine hydrochloride is a water-soluble salt which is injected or taken by nasal inhalation, “snorted”.

- Although cocaine hydrochloride is destroyed by heat, it may be chemically converted to a free-base (“crack”) cocaine, which can be smoked. Pulmonary absorption of “crack” is as rapid as IV injection.

- Cocaine’s half-life is short, resulting in the need for frequent administration; active cocaine users may inject or inhale cocaine as many as 20 times a day.

- Cocaine induces feelings of elation, omnipotence and invincibility and with volatile behavior and rapid development of dependence.

- Cocaine use is associated with high risk sexual behavior.
Site of Cocaine Binding
Disulfiram

- Increases dopamine in the brain by inhibiting dopamine beta hydroxylase.
- 6 RCTs have demonstrated efficacy in treating cocaine dependence.
- Dosage: 250 mg/day
- No studies in HIV/HCV populations so need to watch AST/ALT
- Problem remains adherence. Works well with the motivated patient or the patient who is administered it with methadone.
Pharmacology in Primary Care: Methamphetamine = Bupropion
Methamphetamine (MA)

- MA is a psychostimulant similar in chemical structure to amphetamine with more profound effects on the CNS and can be smoked, snorted, injected, or administered rectally.
- Produces stimulation and feelings of euphoria and has a long duration of action (6 to 8 hours after a single dose)
- Tolerance develops rapidly and escalation of dose and frequency is required.
- As with cocaine, MA use is associated with high risk sexual behavior (especially in MSM)
- Neurocognitive effects of MA use worse in HIV positive patients.
Dopamine Transporters in Methamphetamine Abusers

Motor Task
Loss of dopamine transporters in the meth abusers may result in slowing of motor reactions.

Memory task
Loss of dopamine transporters in the meth abusers may result in memory impairment.

Treatments

- Bupropion 150 mg twice daily has shown some reduction in use among mild methamphetamine users (Shoptaw, DAD. 2008)
- Counseling remains the mainstay
Pharmacology in Primary Care: Alcohol = Naltrexone
Alcohol Main Points

- Disinhibition that leads to increased risk-taking behaviors and poor adherence to all treatments
- Withdrawal seizures
- The drug that really is frightening because it is neurotoxic and accelerates HCV disease progression
- CAGE Questions
ETOH Treatment

- **Naltrexone**
  - FDA approved and standard of care
  - Watch for hepatotoxicity (black box warning)
  - Dosages: 100 mg per day (based on COMBINE study)

- **Acamprosate**
  - FDA approved, but inferior to naltrexone

- **Disulfiram**
  - FDA approved, but inferior to naltrexone
Topiramate

- Not FDA approved for ETOH dependence
- 8 papers showing efficacy of topiramate for ETOH dependence
- Doses varied by trial, but typically patients were started low (25 mg daily) and titrated up to a max of 300 mg over 6 weeks.
- Important choice because:
  1. Can give to patients on opioids
  2. Moderates symptoms of withdrawal
Pharmacology in Primary Care: Nicotine = Nicotine
The 5 A’s

- Ask about tobacco use
- Advise smokers to quit
- Assess willingness to quit
- Assist with quitting
- Arrange follow-up

• Brief advice to quit does make a difference!
Pharmacotherapy

- Nicotine replacement helps
- Bupropion doubles quit rates (but is metabolized by CYP 2B6 so possible interactions with NFV, RTV, and EFV). Doses 150 mg to 300 mg effective.
- Varenicline – better than bupropion and nicotine in comparison trials – watch for suicidality and exacerbation of neuropsychiatric symptoms. Slow upward titration to minimize side effects.
Continuum of Interventions

Knowing the Pieces
Range of Treatments

- **Risk (Harm) Reduction**
  - Decrease frequency of adverse events related to a behavior
  - Change in use behavior – e.g., Changing from injection use to sniffing

- **Risk (Harm) Removal**
  - Cessation of substance abuse
  - Abstinence based – 12 Steps
  - Agonist based – buprenorphine, methadone
Harm reduction is critical because drug addiction is a chronic illness with relapse rates similar to those of hypertension, diabetes, and asthma.

McLellan et al., JAMA, 2000.
Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses

- Drug Addiction: 40 to 60%
- Type I Diabetes: 30 to 50%
- Hypertension: 50 to 70%
- Asthma: 50 to 70%

McLellan et al., JAMA, 2000.
There is a right way and a wrong way to measure the outcome of treating chronic illnesses like addiction.
DAT Recovery with prolonged abstinence from methamphetamine

There is hope!!
Questions?

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