Prescription Opioids

“An Introduction and Overview of Pharmacology and Effects”

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Webinar and online course are co-sponsored by the Pennsylvania Certification Board (PCB)
Learning Objectives:

- Identify the various opioid medications prescribed and their pharmacological differences and similarities.
- Understand the neurochemical affects of opioids on the brain and the resulting symptoms.
- Understand the use of opioid medications in the treatment of opiate dependency, and the neurochemical and pharmacological principles at work.
Why Are We Here Today?

- Treatment admissions for opiates other than heroin rose from 19,870 in 1998 to 111,251 in 2008 – a 450% increase! *
- In 2009:
  - 7 million Americans reported current (past month) nonmedical use of prescription drugs – more than the number using cocaine, heroin, hallucinogens, and inhalants combined.**
  - 2.2 million Americans use pain relievers nonmedically for the first time; initiates of marijuana use were at 2.4 million.**

* SAMHSA, Office of Applied Studies, TEDS data, April 2010
** SAMHSA, Results of 2009 National Survey on Drug Use and Health: National Findings, HHS Publication No. SMA 10-4586FIndings
In 2009, 1.2 million ED visits involved the nonmedical use of pharmaceuticals or dietary supplements. The most frequently reported drugs in the nonmedical use category of ED visits were **opiate/opioid analgesics**, present in 50 percent of nonmedical-use ED visits:

- hydrocodone (alone or in combination) in 104,490 ED visits
- oxycodone (alone or in combination) in 175,949 ED visits
- methadone in 70,637 ED visits.
• Workplace insurers spend an estimated $1.4 billion annually on narcotic painkillers, or opioids.

• Sales of painkillers reached about $8.5 billion last year, compared with $4.4 billion in 2001, according to the consulting firm IMS Health.

• Between 2001 and 2008, narcotics prescriptions as a share of all drugs used to treat workplace injuries jumped 63 percent
2009/2010 Most Prescribed Drugs

- #1 Hydrocodone/acetaminophen
  - 128.2 million prescriptions (2009)
  - 131.2 million prescriptions (2010)
  - Average monthly cost of $12
  - Immediate release formulation
  - Apap use dangerous/questioned
In 2009, there were 7 million Americans aged 12 years and older who abused prescription drugs for non-medical purposes within the past month, up from 6.2 million in 2008. This represents a 13 percent increase in just one year.

In 2009, on average, 6,027 persons per day abused prescription pain relievers for the first time. The total number of individuals that initiated drug use with prescription drugs exceeds the number of individuals that initiated drug use with marijuana.

Every day, on average, 2,500 teens use prescription drugs to get high for the first time.

1 in 7 teens admit to abusing prescription drugs to get high in the past year. Sixty percent of teens who abused prescription pain relievers did so before the age of 15.

Fifty-six percent of teens believe that prescription drugs are easier to get than illicit drugs.

2 in 5 teens believe that prescription drugs are “much safer” than illegal drugs. And 3 in 10 teens believe that prescription pain relievers are not addictive.

Sixty-three percent of teens believe that prescription drugs are easy to get from friends’ and family’s medicine cabinet.

According to the Center for Disease Control, prescription drugs, including opioids and antidepressants, are responsible for more overdose deaths than “street drugs” such as cocaine, heroin, and amphetamines.

The number of emergency room visits attributable to pharmaceuticals alone is up 97% between 2004 and 2008.

The number of persons seeking treatment for pain reliever abuse is up more than fourfold between 1998 and 2008.
“Chemical Puzzle”

Pieces of the puzzle include:
- opioids
- neurotransmitters:
  - dopamine
  - GABA
  - serotonin
  - endorphins
Opium Poppy

Contains:
Numerous alkaloids, (naturally occurring chemicals), notably:

MORPHINE  10-15%
CODEINE  1-3%
THEBAINE  1-2%
Raw Opium

Can be smoked in raw form, or processed into morphine, codeine, heroin or other chemicals for pharmaceutical use.
In September, the United Nations Office on Drugs and Crime said the value of Afghan opium rose from $29 per pound in 2009 to $77 per pound last year.
REVIEW OF OPIATES

NATURAL
- Morphine
- Codeine

SEMI-SYNTHETIC
- Diacetylmorphine
- Hydromorphone
- Oxycodone
- Oxymorphone
- Hydrocodone
- Buprenorphine

SYNTHETIC
- Meperidine
- Fentanyl
- Methadone
Natural Opiates

- Morphine
  "Morpheus"
  10-15%
  Discovered in 1803
  Moderate/severe pain
  MS Contin, Kadian, Avinza, Oramorph

- Codeine
  "Poppy Head"
  1-3%
  Discovered in 1832
  Mild/moderate pain,
  Cough
  Tylenol with Codeine
## Semi-synthetic Opiates

- Diacetylmorphine (Heroin)
- Hydromorphone (Dilaudid)
- Oxycodone (Oxycontin, Roxicodone)
- Oxymorphone (Opana)
- Hydrocodone (Vicodin, Lortab)
- Buprenorphine (Suboxone, Subutex)
Synthetic Opiates

- Meperidine (Demerol)
- Fentanyl (Duragesic)
- Methadone (Dolophine)
- Tramadol * (Ultram)

*Tramadol considered a “non-typical opioid”.

Chemical structures are not related to morphine or codeine.
Opioid Chemistry

• Different chemical structure lends to:
  - Varying degrees of absorption outside and inside of the CNS.
  - Varying rates of absorption
  - Varying onset and duration of action
  - Varying receptor affinity
  - Varying degree of side effects
Opiate Chemistry
Morphine molecule  Codeine molecule
Semi-synthetic Opiates

- Morphine
- Diacetylmorphine
- Oxymorphone
- Hydromorphone
Semi-synthetic Opiates

Codeine → Oxycodone → Hydrocodone
Semi-synthetic Opiates

Thebaine  
Buprenorphine
Relative Strengths (Analgesic Potency)

- Morphine 1.0
- Codeine 0.5 (metabolism)
- Hydrocodone 0.6 (metabolism)
- Oxycodone 2.0
- Hydromorphone 7-11
- Oxymorphone 7.0
- Buprenorphine 40
- Methadone 7.5
- Fentanyl 50-100
Morphine

- Moderate to severe pain relief
- Active and available for oral and IV administration.
- IR active in 30 min.
- ER active in 90 min.
- Moderate bioavailability (40%)
- Histamine release and nausea/vomiting
Codeine

-Mild to moderate pain relief, cough suppression
-Active only orally
-IR active in 30 min.
-No long acting product
-Moderate bioavailability (50%)
-Histamine release and nausea/vomiting
-Manufactured in combination with APAP
Diacetylmorphine

- Low oral bioavailability, better through insufflation, best absorption IV
- Metabolizes to morphine once in the CNS
- Provides “rush” by entering brain very quickly.
- Large amount of histamine release with IV
Hydrocodone

- Mild to moderate pain relief
- Active only orally
- IR active in 30 min.
- No long acting product
- Good bioavailability (70%)
- Manufactured in combination with APAP
**Oxycodone**

- Moderate to severe pain relief
- Active only orally
- IR (Roxicodone)
- ER (Oxycontin)
- Very good bioavailability (80+%)
- Manufactured alone or in combination with APAP (Percocet)
- Multiple receptor site activity
Hydromorphone

- Severe pain relief
- Active orally and IV, IM (highly water soluble)
- Highly reactive with mu receptor
- IR products, ER products newer
- Good bioavailability, excellent penetration in the Blood Brain Barrier
Oxymorphone
- Severe pain relief
- Available as orally active products in IR (generics) ER (Opana)
- Highly reactive with the mu receptor
- Resistant to several metabolic processes, provides extended action.
Buprenorphine

- Moderate to severe pain relief, opiate dependence treatment
- High lipid solubility
- Partial agonist/antagonist activity
- Long acting drug due to affinity at receptor sites
Fentanyl
- Severe pain relief
- Fully synthetic
- Most potent opioid available
- Highly lipophilic (excellent penetration of the Blood Brain Barrier)
- Fast acting, short duration chemistry
Methadone
- Moderate to severe pain relief, opiate dependence treatment
- Fully synthetic
- High but variable bioavailability (40 to 100%)
- Variable metabolism
- High tissue binding
- Enzyme induction
- Long $T \frac{1}{2}$ compared to activity
Meperidine

- Moderate to severe pain relief
- First synthetic opiate
- Weak mu receptor activity
- Antispasmodic activity
- Neurotoxic concerns
- Rapid onset of action
Tramadol

- *Atypical* opioid, chemical analogue of codeine
- Available as IR and ER formulation
- Metabolite has much greater affinity and selectivity for *mu* receptor
- High oral bioavailability
- Noncontrolled substance
Opioid Pharmacology

• Pharmacology helps to explain the effects and symptoms produced by drugs in the body. (Indications, side effects, tolerance, withdrawal)

• Pharmacokinetics involves study of the processes of absorption, distribution, metabolism and elimination. (Half-life, onset of action, duration of action, route of administration)
Opioid Pharmacokinetics

- Onset of action is
  - Immediate by IV route
  - Rapid by IM and PO route
- Peak action occurs in 15 minutes to 2 hours, depending on drug and route
- Duration of action is from 2 to 8 hours
<table>
<thead>
<tr>
<th>Kinetic Parameters (Chart)</th>
<th>oral bio-availability (avg)</th>
<th>onset of effect</th>
<th>average half life (hr.)</th>
<th>plasma protein binding</th>
<th>typical duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>70-90%</td>
<td>45-60m</td>
<td>prodrug</td>
<td>7-25%</td>
<td>4-6h</td>
</tr>
<tr>
<td>pethidine</td>
<td>40-60%</td>
<td>20-40m</td>
<td>3.5h</td>
<td>60-80%</td>
<td>2-4h</td>
</tr>
<tr>
<td>morphine</td>
<td>30-40%</td>
<td>30-45m</td>
<td>2-4h</td>
<td>35%</td>
<td>3-4h</td>
</tr>
<tr>
<td>oxycodone</td>
<td>60-80%</td>
<td>45-60m</td>
<td>3.5h</td>
<td>45%</td>
<td>4-6h</td>
</tr>
<tr>
<td>hydrocodone</td>
<td>60-80%</td>
<td>45-60m</td>
<td>3.5h</td>
<td>unknown</td>
<td>4-6h</td>
</tr>
<tr>
<td>hydromorphone</td>
<td>24%</td>
<td>30m</td>
<td>2.6h</td>
<td>8-19%</td>
<td>2-3h</td>
</tr>
<tr>
<td>oxymorphone</td>
<td>10%</td>
<td>20-40m</td>
<td>1.3h</td>
<td>10-12%</td>
<td>3-4h</td>
</tr>
<tr>
<td>levorphanol</td>
<td>~50%</td>
<td>20-40m</td>
<td>11-16h</td>
<td>40%</td>
<td>4-8h</td>
</tr>
<tr>
<td>methadone</td>
<td>80%</td>
<td>60-90m</td>
<td>22h</td>
<td>80-90%</td>
<td>6-12h</td>
</tr>
<tr>
<td>fentanyl</td>
<td>-10-15%</td>
<td>10-20m</td>
<td>3.5h</td>
<td>85%</td>
<td>1-2h</td>
</tr>
<tr>
<td>buprenorphine</td>
<td>~10-15%</td>
<td>60m</td>
<td>36h</td>
<td>96%</td>
<td>4-12h</td>
</tr>
<tr>
<td>tramadol</td>
<td>70%</td>
<td>60-90m</td>
<td>6-7h</td>
<td>20%</td>
<td>4-6h</td>
</tr>
<tr>
<td>tapentadol</td>
<td>30-40%</td>
<td>30-45m</td>
<td>4.5h</td>
<td>20%</td>
<td>2-4h</td>
</tr>
</tbody>
</table>
ER, XR, SR, TR

SODAS TECHNOLOGY HIGHLIGHTS

50% immediate-release beads and 50% delayed-release beads

Dexmethylphenidate layer
Inactive core
Polymer coating

Immediate-release bead
Delayed-release, polymer-coated bead

How the delayed-release beads work:
1. Over 4 hours, fluid creates small pores through polymer coating
2. Fluid enters and dissolves the dexmethylphenidate layer
3. This provides a second release of dexmethylphenidate equivalent to the immediate release
Opioid Neurochemistry

- Brain structure
- Neuron structure
- Electrical transmission
- Chemical signaling
- Neurotransmitters
Opioid Effects

- Analgesia
- Euphoria
- Sedation
- Nausea/Vomiting/Constipation
- Depress Cough Reflex
- Effects on Mood and Reward
- Endocrine Effects
- Respiratory depression
- Pruritis
- Miosis
Neurochemistry

- Discovery of *mu* receptor and *endorphins*
- Subsequent discovery of *delta* and *kappa* receptors

<table>
<thead>
<tr>
<th>Mu receptor</th>
<th>Delta receptor</th>
<th>Kappa receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mu 1 – Analgesia</td>
<td>Analgesia</td>
<td>Analgesia, sedation, miosis, respiratory depression, euphoria, dysphoria</td>
</tr>
<tr>
<td>Mu 2 – Sedation, vomiting, respiratory depression, pruritis, euphoria, urinary retention, dependence</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Neurotransmitters

• Gamma - aminobutyric acid (GABA)....inhibitory
• Dopamine....pleasure, reward, memory
• Endorphins....pain relief
• Glutamate....pain transmission
• Substance P....pain transmission, vomiting center
• Serotonin....pain pathway
• Norepinephrine....pain pathway
Areas of Brain

- **Mesolimbic Pathway “Reward Pathway”**
  - Includes the VTA (ventral tegmental area, amygdala, hippocampus, nucleus accumbens, prefrontal cortex.
    - DA, NE, 5-HT in high concentrations
    - Memory, reward, judgment, sensations, movement, coordination
    - Complex interaction of NTs
Dopamine Pathways

- Functions
  - Reward (motivation)
  - Pleasure, euphoria
  - Motor function (fine-tuning)
  - Compulsion
  - Perseveration

Serotonin Pathways

- Functions
  - Mood
  - Memory processing
  - Sleep
  - Cognition

Frontal cortex

Stratum

Substantia nigra

Nucleus accumbens

VTA

Hippocampus

Raphe nucleus

NIDA
Receptor Site Evolution
Opioid Receptor Activity

- Agonist
- Antagonist
- Partial agonist

**Affinity**: Strength of the interaction between drug and receptor

**Efficacy**: Measure of the strength of activity or effect from interaction
Opioid Agonists

- Most opiates are agonists, stimulating the mu, delta and kappa receptors.
- Relative affinity and genetic differences in receptor sensitivity account for varying activity.
- High affinity and efficacy
Opioid Partial Agonists

• High \textit{affinity} and \textit{low efficacy} at the \textit{mu} receptor. Diminished activity of other opiates.

• High \textit{kappa receptor antagonist} activity for analgesia and abuse deterrence.

• High \textit{kappa receptor} activity leads to ceiling effect of analgesia and certain side effects.

• Buprenorphine
Opioid Antagonists

- High **affinity** and **no efficacy** at the mu, kappa and delta receptors. Diminished activity of other opiates.
- Oral (naltrexone) and parenteral (naloxone) uses.
- Combined with other opiates (buprenorphine:naloxone)
Opioid Metabolism

- Liver enzymes account for metabolic breakdown of substances
- Thousands of different enzymes have been identified
- Huge variation in individuals (genetics, gender, age, diet, disease state, drug interactions)
- Opioid metabolism results in the production of both inactive and active metabolites. In fact, active metabolites may be more potent than the parent compound.
<table>
<thead>
<tr>
<th>Opioid</th>
<th>Phase 1 metabolism</th>
<th>Phase 2 metabolism</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>None</td>
<td>Glucuronidation via UGT2B7</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>CYP2D6</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>CYP2D6</td>
<td>None</td>
<td>One of the metabolites of hydrocodone is hydromorphone, which undergoes phase 2 glucuronidation</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>CYP3A4</td>
<td>None</td>
<td>Oxycodone produces a small amount of oxymorphine, which must undergo subsequent metabolism via glucuronidation</td>
</tr>
<tr>
<td>Methadone</td>
<td>CYP3A4</td>
<td>None</td>
<td>CYP3A4 and CYP2B6 are the primary enzymes involved in methadone metabolism; other enzymes play a relatively minor role</td>
</tr>
<tr>
<td>methadone</td>
<td>CYP2B6</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>methadone</td>
<td>CYP2C8</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>methadone</td>
<td>CYP2C19</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>tramadol</td>
<td>CYP3A4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>tramadol</td>
<td>CYP2D6</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>fentanyl</td>
<td>CYP3A4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>None</td>
<td>Glucuronidation via UGT2B7</td>
<td></td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>None</td>
<td>Glucuronidation via UGT2B7</td>
<td></td>
</tr>
</tbody>
</table>

CYP = cytochrome P450; UGT2B7 = uridine diphosphate glucuronosyltransferase 2B7.
<table>
<thead>
<tr>
<th>Opioid</th>
<th>Inactive metabolites</th>
<th>Active metabolites identical to pharmaceutical opioids</th>
<th>Active metabolites that are not pharmaceutical opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Normorphine</td>
<td>Hydromorphone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Morphine-3-G glucuronide</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Minor metabolites</td>
<td>None</td>
<td>Hydromorphone-3-glucuronide</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Norhydrocodone</td>
<td>Hydromorphone</td>
<td>None</td>
</tr>
<tr>
<td>Codeine</td>
<td>Norcodeine</td>
<td>Hydrocodone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>None</td>
<td>Oxymorphone</td>
<td>Noroxycodone</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Oxymorphone-3-glucuronide</td>
<td></td>
<td>6-Hydroxy-oxymorphone</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Norfentanyl</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Nortramadol</td>
<td>None</td>
<td>O-desmethy tramadol</td>
</tr>
<tr>
<td>Methadone</td>
<td>2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrroline</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Heroin</td>
<td>Normorphine</td>
<td>Morphine</td>
<td>6-Monoacetylmorphine</td>
</tr>
</tbody>
</table>

<sup>a</sup> Only very low levels are seen in the urine: less than 11% for hydrocodone after codeine administration and less than 2.5% for hydromorphone after morphine administration. <sup>53,54,58</sup>
Treatment Implications

- Tolerance and Dependence
- Detoxification
- Short – Term Withdrawal
- Long – Term Withdrawal
- Medication Maintenance Therapy
- Drug Free Possibilities
Back to the Mesolimbic Brain

Dopamine Pathways

- Frontal cortex
- Functions
  - Reward (motivation)
  - Pleasure, euphoria
  - Motor function (fine-tuning)
  - Compulsion
  - Perseveration

Serotonin Pathways

- Striatum
- Substantia nigra
- Functions
  - Mood
  - Memory processing
  - Sleep
  - Cognition

Nucleus accumbens
VTA
Hippocampus
Raphe nucleus

NIDA
Neurochemistry of Addiction

- In the absence of pain, reward processes are continuously activated by opioids
- VTA stimulation by opioids increases dopamine release from the Nucleus Accumbens
- Memory circuits are stimulated also, causing associations to form
Opioid Tolerance

- **Mu receptors** become less responsive
- **Receptors** become less available (*down regulation*)
- **NMDA receptor antagonists** and **glutamate**
- Involvement with the **Locus coeruleus (LC)** part of the brain, and **norepinephrine** output
- Impact of opioids is offset over time by adjusting mechanisms of neurons
<table>
<thead>
<tr>
<th>Normal</th>
<th>Opioid Induced</th>
<th>Opioid Removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate levels of NE</td>
<td>Reduced levels of NE</td>
<td>Excessive levels of NE</td>
</tr>
<tr>
<td>Wakefulness</td>
<td>Drowsiness</td>
<td>Anxiety/Wakefulness</td>
</tr>
<tr>
<td>Breathing</td>
<td>Reduced Respiration</td>
<td>Increased Respiration</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Low Blood Pressure</td>
<td>High Blood Pressure</td>
</tr>
</tbody>
</table>
Signs/Symptoms of Acute Opioid Intoxication

- Constricted pupils
- Euphoria
- Apathy
- Drowsiness
- Loss of consciousness
- Coma
- Psychomotor agitation or retardation
- Decreased respiration
- Decreased heart rate
- Pulmonary edema
- Impaired social judgment
- Slurred speech
- Impaired attention and memory
- Impaired occupational functioning
Opioid Withdrawal Symptoms

- Dilated pupils
- Rhinorrhea
- Epiphora/lacrimation
- Piloerection
- Nausea
- Vomiting
- Diarrhea
- Yawning
- Muscle cramps
- Restlessness
- Elevated vital signs
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Scores</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting pulse rate</td>
<td>0-4</td>
<td>0=80 or less; 1=81-100; 2=101-120; 4=120 or greater</td>
</tr>
<tr>
<td>Sweating</td>
<td>0-4</td>
<td>0=none; 4=sweat streaming from face</td>
</tr>
<tr>
<td>Restlessness</td>
<td>0-5</td>
<td>0=sits still; 5=unable to sit still (even for a few seconds)</td>
</tr>
<tr>
<td>Pupil size</td>
<td>0-5</td>
<td>0=normal; 5=dilated (only iris rim visible)</td>
</tr>
<tr>
<td>Bone or joint aches</td>
<td>0-4</td>
<td>0=none; 4=severe discomfort</td>
</tr>
<tr>
<td>Runny nose or tearing</td>
<td>0-4</td>
<td>0=none; 4=constant</td>
</tr>
<tr>
<td>GI upset</td>
<td>0-5</td>
<td>0=none; 5=multiple episodes of vomiting or diarrhea</td>
</tr>
<tr>
<td>Tremor</td>
<td>0-4</td>
<td>0=none; 4=gross tremor</td>
</tr>
<tr>
<td>Yawning</td>
<td>0-4</td>
<td>0=none; 4=yawning several times/minute</td>
</tr>
<tr>
<td>Anxiety &amp; Irritability</td>
<td>0-4</td>
<td>0=none; 4=severe, precluding participation</td>
</tr>
<tr>
<td>Gooseflesh skin</td>
<td>0-5</td>
<td>0=smooth; 5=prominent piloerection</td>
</tr>
</tbody>
</table>

COWS=Clinical Opiate Withdrawal Scale; GI=gastrointestinal.
Score: 5-12 mild; 13-24=moderate; 25-36=severe.
Goals of Opioid Replacement Therapy

• Detoxification
  - Prevent fatal results
• Stabilization
  - Address acute withdrawal
• Maintenance
  - Address long term withdrawal
• Completion (Drug-free)
  - Use of drug taper to minimize withdrawal
Opioid Replacement Therapy
“Corrective, not Curative”

- Methadone
- Buprenorphine
Methadone

- Schedule II Drug
- Treatment use since 1964
- Full agonist at the mu receptor
- Synthetic drug
- Slow rate of metabolism, highly lipid soluble
- Long-acting, long half-life (15 – 60 hrs)
- Diffuses into multiple body tissue
- Once daily dosing schedule
Methadone
Methadone (cont)

- Relapse rates a function of:
  - Dose of medication
  - Length of time in treatment
  - Polydrug use
  - Policies of program
Buprenorphine

- Schedule III Drug
- Treatment use since 2002 (DATA 200)
- *Partial agonist* at the *mu receptor*
- Long half life (24-60 hrs)
- Semi-synthetic drug
- *Sublingual* administration
- Prescriber regulations
- *Ceiling Effect* of 32mg dose
Buprenorphine
Average Half life of a 16mg. dose of buprenorphine

Effective dose (mgs.)

Hours since a single 16mg dose, taken all at once
Effects of the average half life of 16mgs/day of buprenorphine (Stabilization)

Effective "onboard" total dose (mgs.)

Hours since 1st 16mg. dose

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Buprenorphine (cont)

- Suboxone formulations include \textit{naloxone} in a 4:1 ratio to deter diversion for IV use
  
  Buprenorphine 8mg:naloxone 2mg
  Buprenorphine 2mg:naloxone 0.5mg

- Effectiveness questioned

- “Subs” have a definite street market and value

- Programs evolving to address psychosocial needs of patients
Buprenorphine Treatment

- **The induction phase** is the medically monitored startup of buprenorphine therapy. Buprenorphine for induction therapy is administered when an opioid-addicted individual has abstained from using opioids for 12–24 hours and is in the early stages of opioid withdrawal. If the patient is not in the early stages of withdrawal (i.e., if he or she has other opioids in the bloodstream), then the buprenorphine dose could precipitate acute withdrawal.
Buprenorphine Treatment

- **The stabilization phase** has begun when a patient has discontinued or greatly reduced the use of his or her drug of abuse, no longer has cravings, and is experiencing few or no side effects. The buprenorphine dose may need to be adjusted during the stabilization phase. Because of the long half-life of buprenorphine it is sometimes possible to switch patients to alternate-day dosing once stabilization has been achieved.
Buprenorphine Treatment

• **The maintenance phase** is reached when the patient is doing well on a steady dose of buprenorphine (or buprenorphine/naloxone). The length of time of the maintenance phase is individualized for each patient and may be indefinite.
• If you are interested in learning more about buprenorphine both as a treatment and detoxification medication, IRETA is offering a free online learning opportunity for the next month - via the online learning portal at ireta.org.
• There you will be able to access two separate and distinct courses-

• “Buprenorphine Treatment: A Training for Multidisciplinary Addiction Professionals”

• "Short-term Opioid Withdrawal Using Buprenorphine."
• The online course is completely optional
• June 27, 2012 through July 31, 2012
• Free CEUs available

Thank You!