

# BUPRENORPHINE TREATMENT

## Curriculum Infusion Package (CIP) For Infusion Into Undergraduate Pharmacology Courses

**A Pharmacology Course  
Developed by Mountain West ATTC**



In order to disseminate information to the addiction treatment field, the National Institute on Drug Abuse (NIDA) has created a partnership with the Addiction Technology Transfer Center (ATTC) Network funded by the Substance Abuse and Mental Health Services Administration (SAMHSA). The fourteen regional ATTCs throughout the country and the ATTC National Office provide specialized training and technical assistance to substance abuse treatment professionals in order to create a more effective treatment workforce. Through the NIDA-SAMHSA Blending Initiative, special groups called Blending Teams composed of NIDA researchers and ATTC representatives meet to design dissemination strategies.

Based off the Buprenorphine Awareness initiative package, Mountain West ATTC has created this Curriculum Infusion Package (CIP) to educate about buprenorphine and its use in the treatment of opioid addiction.

# NIDA-SAMHSA Blending Initiative: Blending Team Members

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## **Team Members**

The membership consisted of three ATTC representatives and three NIDA researchers.

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- The O.A.S.I.S. Clinic developed and granted permission for inclusion of the video, “Put Your Smack Down! A Video about Buprenorphine.”



# Topics included this Curriculum Infusion Package (CIP)

We will review the following:

- Prevalence of opioid use in the U.S.
- Identify groups of people who are using opioids
- Understand how buprenorphine will benefit the delivery of opioid treatment
- Opioid pharmacology
- Descriptions and definitions of opioid agonists, partial agonists, and antagonists
- Opioid addiction and the brain
- Advantages and disadvantages of Buprenorphine



## Prevalence of Opioid Use and Abuse in the United States



So how significant is the problem of opioid use in the U.S.? Let's look at some of the available statistics.

## Who Uses Heroin?

Individuals of all ages use heroin:

- More than 3 million US residents aged 12 and older have used heroin at least once in their lifetime.
- Heroin use among high school students is a particular problem. Nearly 2 percent of US high school seniors used the drug at least once in their lifetime, and nearly half of those injected the drug.

SOURCE: National Survey on Drug Use and Health; Monitoring the Future Survey.

More than 3 million people over the age of 12 have used heroin at least one time.

Among high school students:

- Almost 2% have used heroin at least once.
- Almost half of those who had tried it had injected the drug.

## Initiation of *Heroin Use*

- During the latter half of the 1990s, the annual number of heroin initiates rose to a level not reached since the late 1970s.
- In 1974, there were an estimated 246,000 heroin initiates.
- Between 1988 and 1994, the annual number of new users ranged from 28,000 to 80,000.
- Between 1995 and 2001, the number of new heroin users was consistently greater than 100,000.

SOURCE: SAMHSA, National Survey on Drug Use and Health, 2002.

The number of new people initiating heroin use has also increased to a level comparable to that seen 30 years ago.

In 1974, there were 246,000 new heroin users.

That number dropped to between 28,000-80,000 between 1988 and 1998.

Between 1994 and 2001, the number of new heroin initiates was about 100,000 per year.

# Treatment Admissions for Opioid Addiction

Another indicator of a drug problem is to look at the number and demographics of people seeking treatment for particular drugs. These data will provide another way to look at the populations affected by particular drugs.

## Who Enters Treatment for *Heroin Abuse?*

- 90% of opioid admissions in 2000 were for heroin
- 67% male
- 47% White; 25% Hispanic; 24% African American
- 65% injected; 30% inhaled
- 81% used heroin daily

SOURCE: SAMHSA, Treatment Episode Data Set, 1992-2000.

- In 2000, 90% of all admissions for opioid treatment were for heroin.
- People entering treatment were 2/3 male; just under half were White, 1/4 were Hispanic, and 1/4 were African American; 2/3 of the people seeking treatment used by injection; and 4 out of 5 used heroin on a daily basis.

## Who Enters Treatment for *Heroin Abuse?*

- 78% had at least one prior treatment episode; 25% had 5+ prior episodes
- 40% had a treatment plan that included methadone
- 23% reported secondary alcohol use; 22% reported secondary powder cocaine use

SOURCE: SAMHSA, Treatment Episode Data Set, 1992-2000.

- Approximately 3/4 of those entering treatment for heroin in 2000 had at least one prior treatment episode, and 1/4 had 5 or more previous episodes.
- 40% were seeking treatment that included methadone.
- Secondary drug use among people seeking treatment for heroin addiction included alcohol (23%) and cocaine (22%).

## Who Enters Treatment for *Other Opiate Abuse?*

**(Non-prescription use of methadone, codeine, morphine, oxycodone, hydromorphone, opium, etc.)**

- 51% male
- 86% White
- 76% administered opiates orally
- 28% used opiates other than heroin after age 30
- 19% had a treatment plan that included methadone
- 44% reported no secondary substance use; 24% reported secondary alcohol use

SOURCE: SAMHSA, Treatment Episode Data Set, 1992-2000.

- Among people seeking treatment for abuse of other opiates, 1/2 were male, the great majority (86%) was White; and 3/4 took the drug orally.
- One in five had a treatment plan that included methadone.
- 44% reported no use of other drugs, and 24% reported alcohol use.

## Four Reasons for Not Entering Opioid Treatment

1. Limited treatment options
  - Methadone or Naltrexone
  - Drug-Free Programming
2. Stigma
  1. Many users don't want methadone
    - "It's like going from the frying pan into the fire"
    - Fearful of withdrawing from methadone
  2. Concerned about being stereotyped
3. Settings have been highly structured
4. Providers subscribe to abstinence-based model

The previous information clearly indicates that opioid use has been increasing, and that a large number of people are seeking treatment for opioids. Data have also been collected that indicate that there are many more users of heroin than people seeking and/or receiving treatment.

This raises the question: why are some people not entering treatment?

#1: The current treatment system involves either a medicalized model (e.g., the opioid treatment programs) or psychosocial programming. Many Opioid Treatment Programs (OTPs) do not have large behavioral treatment components and many psychosocial programs do not provide adequate medical intervention to help the person through the withdrawal process.

#2: Anecdotal evidence exists to suggest that people may feel that getting off methadone is much harder than getting off heroin. Lack of understanding about how methadone should be used, as well as the possibility for illicit use of methadone, contributes to this feeling. Additionally, people are afraid of being labeled and stereotyped due to their opioid addiction (e.g., "junkies").

#3. Opioid treatment programs (OTPs) have very structured rules requiring regular attendance. Programs often open early in the morning and close by mid-afternoon. Clients who are not able to follow the rules or attend the program during operating hours may not be able to receive the treatment.

#4: Many providers believe that treatment requires abstinence from all drugs. However, many opioid users are not able to stop using opioids. They often cannot tolerate the withdrawal experience, and even if they can, may be drawn back to using. Using a medication such as methadone or buprenorphine to assist with the withdrawal process or to prevent people from going through withdrawal will help them to participate in treatment and function more normally in their daily lives.

## A Need for Alternative Options

- Move outside traditional structure to:
  - Attract more patients into treatment
  - Expand access to treatment
  - Reduce stigma associated with treatment
- Buprenorphine is a potential vehicle to bring about these changes.

Drug Addiction Treatment Act 2000 (DATA 2002) allows for a new treatment option by expanding treatment options to include both the general health care system and opioid treatment programs (OTPs). Opioid treatment will continue to be offered through OTPs as it has been in the past. Data 2000 allows for expansion beyond the structure in place for methadone to allow for treatment in physician offices. By doing so:

- More patients may be willing to seek treatment;
- More patients will have access to treatment; and
- Stigma may be reduced by broadening the definition and locations of available treatment options.

## Buprenorphine: An Exciting New Option

Buprenorphine represents an exciting addition to the available opioid treatment options.

## Development of Tablet Formulations of Buprenorphine

- Buprenorphine is marketed for opioid treatment under the trade names of Subutex® (buprenorphine) and Suboxone® (buprenorphine/naloxone)
- Over 25 years of research
- Over 5,000 patients exposed during clinical trials
- Proven safe and effective for the treatment of opioid addiction

**Subutex®** = a sublingual tablet containing buprenorphine hydrochloride only

**Suboxone®** = a sublingual tablet containing both buprenorphine hydrochloride and naloxone hydrochloride in a 4:1 ratio

**Suboxone®** is the focus of U.S. marketing efforts, even though both formulations are available in the U.S.

These medications have a tremendous amount of research behind them to show that they are both safe and effective in the treatment of opioid addiction.

## Moving Science-Based Treatments into Clinical Practice

- A challenge in the addiction field is moving science-based treatment methods into clinical settings.
- NIDA and CSAT initiatives are underway to bring research and clinical practice closer.
- Buprenorphine treatment represents an achievement in this effort.

Many treatments that are developed never make it into real-world practice.

This has been a problem for quite some time and both the National Institute on Drug Abuse (NIDA) and the Substance Abuse Mental Health Services Administration (SAMHSA) have recognized this. The Blending Team that developed these materials resulted from one initiative designed to help move scientific findings into practical application: The NIDA-SAMHSA Blending Initiative.

Buprenorphine is an important treatment advancement and represents an exciting opportunity for individuals to develop strategies to work with both providers and researchers to find ways to make this treatment a readily-available option.

# Buprenorphine: A Science-Based Treatment

Clinical trials have established the effectiveness of buprenorphine for the treatment of heroin addiction. Effectiveness of buprenorphine has been compared to:

- Placebo (Johnson et al. 1995; Ling et al. 1998; Kakko et al. 2003)
- Methadone (Johnson et al. 1992; Strain et al. 1994a, 1994b; Ling et al. 1996; Schottenfield et al. 1997; Fischer et al. 1999)
- Methadone and LAAM (Johnson et al. 2000)

In the development of the medication, the effectiveness of buprenorphine has been compared to that of other medications that are currently available. These studies have shown that buprenorphine treatment:

- Is more effective than placebo; and
- Has similar effectiveness to moderate doses of methadone and LAAM.

## Buprenorphine as a Treatment for Opioid Addiction

- A synthetic opioid
- Described as a mixed opioid agonist-antagonist (or partial agonist)
- Available for use by certified physicians outside traditionally licensed opioid treatment programs

Several factors make buprenorphine a good option for some people.

Buprenorphine is a partial agonist, resulting in a good safety profile for the medication.

With the changes in the treatment legislation, this medication becomes the first available outside of the OTP system. This expands both the availability of and access to treatment.

## The Role of Buprenorphine in Opioid Treatment

- Partial Opioid Agonist
  - Produces a ceiling effect at higher doses
  - Has effects of typical opioid agonists—these effects are dose dependent up to a limit
  - Binds strongly to opiate receptor and is long-acting
- Safe and effective therapy for opioid maintenance and detoxification

The partial agonist properties of the medication are important to understand.

The effects of the medication at lower doses are virtually the same as that of full agonists. However, as the dose is increased, the effects level out for buprenorphine (especially respiratory suppression), where they continue to increase with full agonist medications. This is called a “ceiling effect.” This ceiling effect greatly decreases the risk of overdose when compared to full agonists.

Buprenorphine has a very HIGH affinity for opioid receptors. It displaces morphine, methadone, and other full agonist opioids from the receptor. Additionally, buprenorphine dissociates slowly from the receptor.

This high affinity for and slow dissociation from the receptor result in buprenorphine blocking the effects of other opioids, such as heroin. Additionally, the high affinity and slow dissociation give rise to buprenorphine’s prolonged therapeutic effects.

Clinical trials have demonstrated that buprenorphine is a safe and effective medication for both opioid maintenance and medically assisted withdrawal (detoxification). Additionally, because buprenorphine is very long-acting, dosing can occur on a less-than-daily basis, as infrequently as three times per week.

# Review of Opioid Pharmacology

So let's review some specific information about opioids and the role of buprenorphine in the treatment system. Then we will discuss the critical role of the multidisciplinary team in providing this treatment.



## Opiate/Opioid : What's the Difference?

### Opiate

- A term that refers to drugs or medications that are derived from the opium poppy, such as heroin, morphine, codeine, and buprenorphine.

### Opioid

- A more general term that includes opiates as well as the synthetic drugs or medications, such as buprenorphine, methadone, meperidine (Demerol®), fentanyl—that produce analgesia and other effects similar to morphine.

Throughout this training we are using the term opioid to define the class of drug with which we are dealing. It is important to understand what this term means.

**Opiate** refers only to drugs or medications that are derived directly from the opium poppy. Examples include heroin, morphine, and codeine.

**Opioid** is a broader term referring to opiates and other synthetically-derived drugs or medications that operate on the opioid receptor system and produce effects similar to morphine. Examples include buprenorphine and methadone.

## Basic Opioid Facts

Description: Opium-derived, or synthetics which relieve pain, produce morphine-like addiction, and relieve withdrawal from opioids

Medical Uses: Pain relief, cough suppression, diarrhea

Methods of Use: Intravenously injected, smoked, snorted, or orally administered

Description: All opioids work basically the same way, regardless of their derivation.

Medical Uses: There are benefits to using opioids; they are not just used recreationally.

Methods: Bottom line – you can get opioids into your body in many ways.

## What's What? Agonists, Partial Agonists, and Antagonists

<u>Agonist</u>	Morphine-like effect (e.g., heroin)
<u>Partial Agonist</u>	Maximum effect is less than a full agonist (e.g., buprenorphine)
<u>Antagonist</u>	No effect in absence of an opiate or opiate dependence (e.g., naloxone)

Increasing the dose of a full agonist produces increasing effects until the receptor is fully activated and a maximum effect is reached.

Partial Agonists share some characteristics of full agonists. At low doses, full and partial agonists produce effects that are essentially indistinguishable. However, increasing the dose of a partial agonist DOES NOT produce as great an effect as occurs with a full agonist. There is a CEILING to the agonist (intoxicating/euphoric/respiratory depression) effects.

In individuals who are not physically dependent on opioids, buprenorphine produces typical opioid agonist effects, such as analgesia, sedation, nausea, and dizziness, but these reach a “ceiling” in most individuals with sublingual doses of 24 to 32 mg.

Antagonists also bind to receptors, but rather than activating them, they block the receptors by preventing them from being activated by an agonist.

### **Key and Lock Analogy:**

One can consider an antagonist to be a key that fits snugly into a lock, but does not open it. It also prevents another key from opening the lock. When people take an antagonist and an agonist in combination, they do not feel the agonist effects. Patients who take naltrexone (an antagonist), for example, do not feel the effects of heroin or other agonists.

# Opioid Agonists

- Natural derivatives of opium poppy
  - Opium
  - Morphine
  - Codeine

## Natural Derivatives:

These substances are derived directly from the opium poppy. They are the drugs that we can also call opiates.

# Opium



SOURCE: [www.streetdrugs.org](http://www.streetdrugs.org)

# Morphine



SOURCE: [www.streetdrugs.org](http://www.streetdrugs.org)

# Opioid Agonists

- **Semisynthetics: Derived from chemicals in opium**
  - Diacetylmorphine – Heroin
  - Hydromorphone – Dilaudid<sup>®</sup>
  - Oxycodone – Percodan<sup>®</sup>, Percocet<sup>®</sup>
  - Hydrocodone – Vicodin<sup>®</sup>

## Semisynthetics:

These substances are derived from chemicals extracted from the opium poppy. They also fall into both the opiate and opioid categories.

# Heroin



SOURCE: [www.streetdrugs.org](http://www.streetdrugs.org)

Left-hand side picture – Mexican black tar heroin (mostly used in the Western U.S.)

Right-hand side top picture – South American white heroin (dominates the heroin market east of the Mississippi River)

Right-hand side bottom picture – Mexican brown heroin

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Heroin has been around for a long time and was originally marketed under the Bayer Label as a cough suppressant. This advertisement is from 1897. It is no longer considered to have any medical uses.

# Opioid Agonists



SOURCE: [www.pdrhealth.com](http://www.pdrhealth.com)

# Opioid Agonists

- Synthetics

- Propoxyphene – Darvon<sup>®</sup>, Darvocet<sup>®</sup>
- Meperidine – Demerol<sup>®</sup>
- Fentanyl citrate – Fentanyl<sup>®</sup>
- Methadone – Dolophine<sup>®</sup>
- Levo-alpha-acetylmethadol – ORLAAM<sup>®</sup>

**Synthetics:**

These substances are synthetically manufactured. They are considered opioids, but are NOT opiates.

# Methadone



# Darvocet



SOURCE: [www.methadoneaddiction.net](http://www.methadoneaddiction.net)

# Opioid Partial Agonists

- Buprenorphine – Buprenex<sup>®</sup>, Suboxone<sup>®</sup>, Subutex<sup>®</sup>
- Pentazocine – Talwin<sup>®</sup>

Buprenex<sup>®</sup> is the injectable formulation of buprenorphine approved and marketed for the treatment of pain; it **IS NOT** approved for the treatment of opioid addiction.

Suboxone<sup>®</sup> is the buprenorphine/naloxone combination tablet and Subutex<sup>®</sup> is the buprenorphine-only tablet. Only these two tablet formulations are approved for the treatment of opioid addiction.

Pentazocine (Talwin<sup>®</sup>) is marketed for pain; it **IS NOT** approved for the treatment of opioid addiction.

# Buprenorphine/Naloxone combination and Buprenorphine Alone



This is what the two sublingual buprenorphine tablets look like.

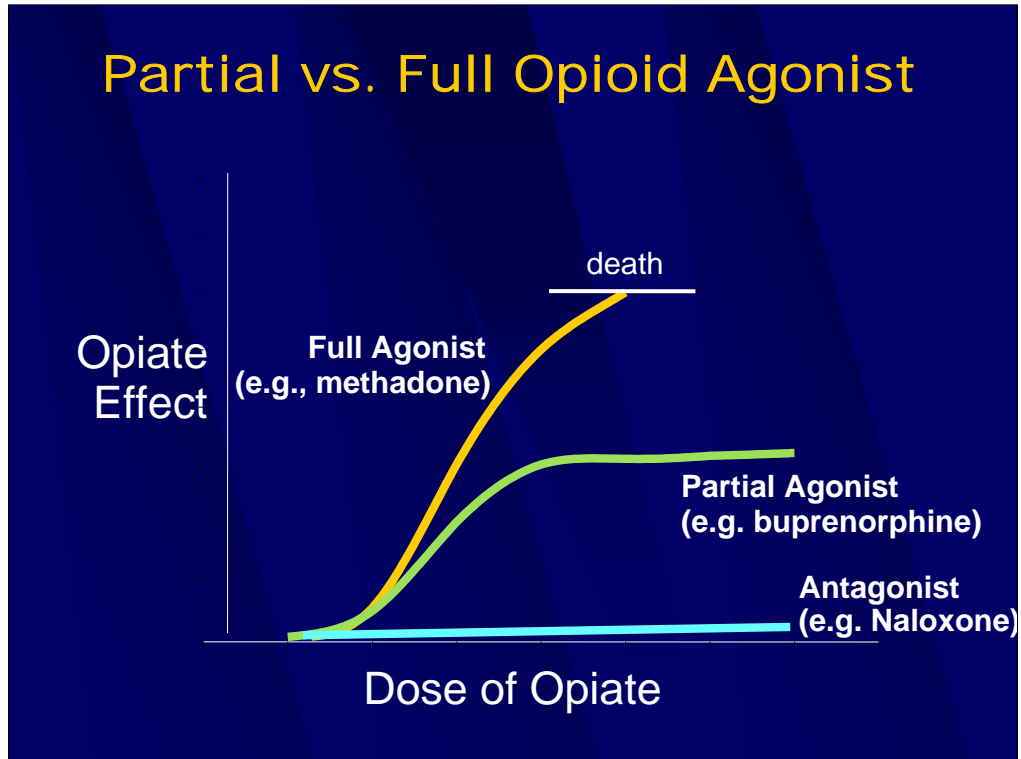
# Opioid Antagonists

- **Naloxone** – Narcan®
- **Naltrexone** – ReVia®, Trexan®



As was previously stated, antagonists are those substances that block the affects of opioid agonists. Two examples are naloxone (the same medication in the buprenorphine/naloxone combination tablet) and naltrexone.

## Partial vs. Full Opioid Agonist



The partial agonist effects of buprenorphine make it much safer at higher doses than full agonists. This is due primarily to the ceiling effect preventing the respiratory suppression seen at higher doses of agonists.

# Opioids and the Brain

So now that you know which drugs and medications are included in the class known as opioids, let's look at how they work.

# Opioid Addiction and the Brain



Opioids attach to receptors in brain → **Pleasure**

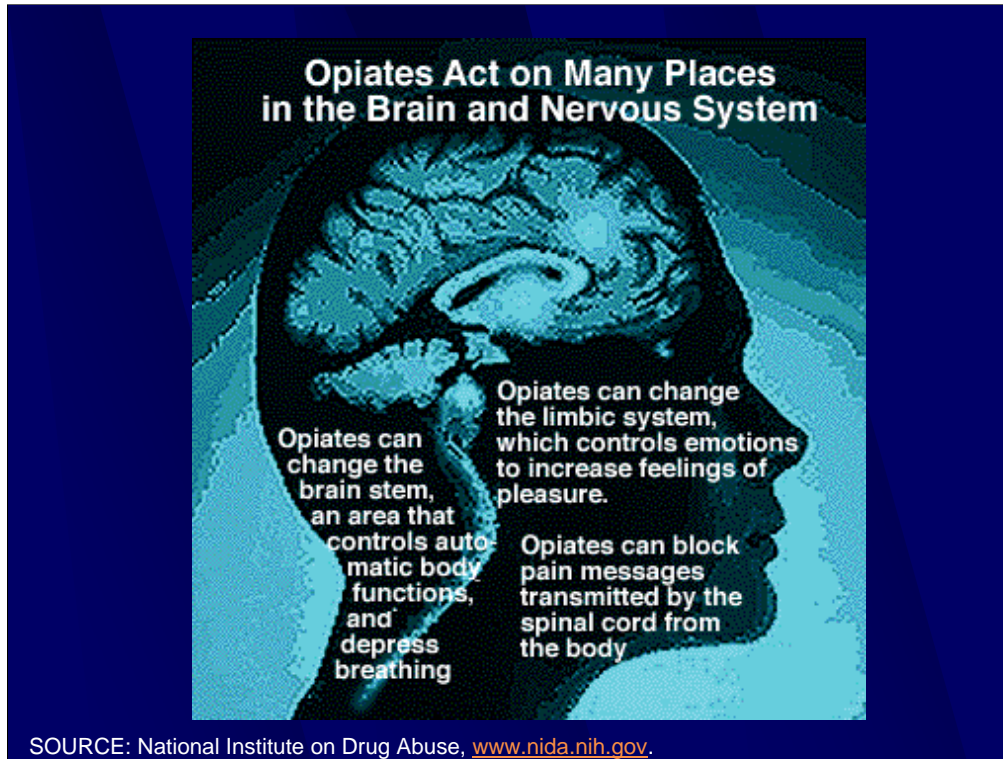
Repeated opioid use → **Tolerance**

Absence of opioids after prolonged use → **Withdrawal**

At first, using opioids results in PLEASURE. But repeated exposure to opioids causes long-lasting changes in brain functioning, resulting in TOLERANCE (a need to keep using more and more in an attempt to feel the pleasure that was once felt).

If you stop using opioids after you've used them for a prolonged period of time, you go through WITHDRAWAL.

Environmental cues associated with drug use activate the brain and cause craving, which often leads back to drug use (RELAPSE).



Opioids affect the brain globally, including areas that control:

- Automatic bodily functions such as breathing, blood pressure, pulse;
- Emotions, especially the areas of the brain responsible for feeling pleasure;
- Pain – opioids block the transmission of pain messages from the body to the brain thereby diminishing or stopping the experience of the pain.

# Terminology

## Receptor:

specific cell binding site or molecule: a molecule, group, or site that is in a cell or on a cell surface and binds with a specific molecule, antigen, hormone, or antibody

Let's take the next few minutes to review some receptor pharmacology-related terms.

## Receptor:

A specific cell or place on a cell to which a specific molecule binds. There are unique receptors for many different molecules, including specific opioid receptors.

# What Happens When You Use Opioids?

- Acute Effects: Sedation, euphoria, pupil constriction, constipation, itching, and lowered pulse, respiration and blood pressure
- Results of Chronic Use: Tolerance, addiction, medical complications
- Withdrawal Symptoms: Sweating, gooseflesh, yawning, chills, runny nose, tearing, nausea, vomiting, diarrhea, and muscle and joint aches

People report that the experience of taking opioids is intensely pleasurable. However, even early in the use cycle, people report negative side effects from use.

Acute effects include the euphoria and sedative effects; people also report constipation, itching, nausea and decreased pulse and respiration.

With chronic use, tolerance and withdrawal symptoms develop and the above symptoms may become more significant.

Withdrawal symptoms from opioids are quite unpleasant and include sweating, runny nose, diarrhea, nausea, and muscle and joint pain.

## Possible Acute Effects of Opioid Use

- Surge of pleasurable sensation = “rush”
- Warm flushing of skin
- Dry mouth
- Heavy feeling in extremities
- Drowsiness
- Clouding of mental function
- Slowing of heart rate and breathing
- Nausea, vomiting, and severe itching

Bullet #1: Rush is generally reported with administration by injection or smoking. It is not commonly associated with oral administration.

Bullet #5: Drowsiness is commonly referred to as “nodding out.”

# Consequences of Opioid Use

- Addiction
- Overdose
- Death
- Use related (e.g., HIV infection, malnutrition)
- Negative consequences from injection:
  - Infectious diseases (e.g., HIV/AIDS, Hepatitis B and C)
  - Collapsed veins
  - Bacterial infections
  - Abscesses
  - Infection of heart lining and valves
  - Arthritis and other rheumatologic problems

The first three consequences (addiction, overdose, and death) refer to opioid use in general. There are also consequences from behaviors that may be associated with substance use such as infections resulting from unprotected sexual behaviors, malnutrition, etc.

Many of the consequences refer specifically to injection drug use:

- Collapsed veins resulting from repeated injections.
  - What do people do if their veins collapse? (*Answer: find another place*).
  - Where besides the bend in the arm might people inject?  
(*Answer: other possible places include between toes/fingers, in the neck, in the thigh, under the tongue, in the groin or genital area*).
- Viral Infections such as HIV or Hepatitis C, resulting from sharing injection equipment with people.
- Bacterial infections may be caused by not cleaning the injection site properly or by using needles that have been exposed to bacteria. This can introduce bacteria to the blood stream.
- An abscess is a subcutaneous infection. If untreated, an abscess can rupture and lead to sepsis or even death.
- Blood infections can be contracted from bacteria transferred into the bloodstream via dirty needles/ syringes. The bacteria settles in the heart, causing an infection of the heart lining (endocarditis) or a breakdown of the heart's valves (which causes them to become less effective at bringing blood to and from the heart).
- Arthritis and other rheumatologic problems may develop as a result of chronic infections and muscle/tissue inflammation.

# Heroin Withdrawal Syndrome

- Intensity varies with level & chronicity of use
- Cessation of opioids causes a rebound in function altered by chronic use
- First signs occur shortly before next scheduled dose
- Duration of withdrawal is dependent upon the half-life of the drug used:
  - Peak of withdrawal occurs 36 to 72 hours after last dose
  - Acute symptoms subside over 3 to 7 days
  - Protracted symptoms may linger for weeks or months

Once the body becomes accustomed to the drug being on board, it may react if the drug is removed. The intensity of the withdrawal symptoms will depend on the level of use (dose and type of opioid) and the frequency and duration of use (chronicity).

Withdrawal symptoms are basically a rebound effect; those functions that have been depressed or altered by the opioid suddenly emerge again.

Withdrawal symptoms are often the opposite of symptoms seen when actively using the opioid (e.g., people get constipated when taking opioids and have diarrhea when withdrawing).

First signs of withdrawal occur shortly after the next scheduled dose.

Length of the withdrawal depends upon the half-life. Opioids with short half-lives (e.g., heroin) have acute withdrawal symptoms that peak at 3-4 days and then subside by days 3-7. Opioids with longer half-lives have longer acute withdrawal periods.

Regardless of the length of the acute withdrawal, there are protracted withdrawal symptoms (e.g., aches and pains, general malaise) that persist for weeks or months after use ceases.

# Opioid Withdrawal Syndrome

## *Acute Symptoms*

- Pupillary dilation
- Lacrimation (watery eyes)
- Rhinorrhea (runny nose)
- Muscle spasms (“kicking”)
- Yawning, sweating, chills, gooseflesh
- Stomach cramps, diarrhea, vomiting
- Restlessness, anxiety, irritability

Acute withdrawal symptoms are the opposite of acute intoxication symptoms.

# Opioid Withdrawal Syndrome

## *Protracted Symptoms*

- Deep muscle aches and pains
- Insomnia, disturbed sleep
- Poor appetite
- Reduced libido, impotence, anorgasmia
- Depressed mood, anhedonia
- Drug craving and obsession

Protracted withdrawal symptoms are less severe than the acute symptoms, but are still experienced as extremely disruptive and uncomfortable.

Anorgasmia = inability to have an orgasm

Anhedonia = overall lack of pleasure (everything is gray)

## Treatment of Opioid Addiction

Anyone who takes opioids for a period of time will develop physical dependence on them. For instance, a patient who is taking vicodin over a period of time for pain will experience withdrawal symptoms if they stop taking in suddenly. This does not mean that they are addicted. It just means that their body has adapted to the medication. Generally, the prescribing physician will help the patient gradually taper down on the dose once the medication is no longer needed.

However, if a person has an addiction to opioids—that is lost control over his/her use, and/or developed the problems associated with addiction (whether or not physical dependence is present)—it is unlikely that he/she is going to stop using without some sort of treatment.

Due to the withdrawal symptoms, a person often cannot tolerate the withdrawal experience, and even if they can, may be drawn back to using. Using a medication such as methadone or buprenorphine to assist with the withdrawal process or to prevent people from going through withdrawal will help them to participate in treatment and function more normally in their daily lives.

## Advantages of Buprenorphine in the Treatment of Opioid Addiction

1. Patient can participate fully in treatment activities and other activities of daily living easing their transition into the treatment environment
2. Limited potential for overdose
3. Minimal subjective effects (e.g., sedation) following a dose
4. Available for use in an office setting
5. Lower level of physical dependence

When transitioned onto buprenorphine, patients can participate fully in treatment activities rather than being sick from withdrawal for several days. This means that treatment can begin as soon as they seek it (while motivation is high).

There are no known cases of overdose directly related to buprenorphine. To date, cases in which overdose has occurred involved use of alcohol or other respiratory depressants (e.g., benzodiazepines). *See Johnson, et al. 2003, for a more detailed discussion.*

Patients report minimal sedation following a dose.

The treatment setting can be determined to fit the needs of the patient (OPT or office-based).

## Advantages of Buprenorphine/Naloxone in the Treatment of Opioid Addiction

- Combination tablet is being marketed for U.S. use
- 6. Discourages IV use
- 7. Diminishes diversion
- 8. Allows for take-home dosing

The marketing effort in the U.S. is focused on the combination formulation. This formulation has several advantages, including the following:

- It discourages injection use because, when injected, the naloxone in the product will lead to withdrawal, whereas when taken sublingually as prescribed, it will not have that effect.
- Because of the above point, the combination tablet lowers the likelihood that the medication will be diverted.

## Disadvantages of Buprenorphine in the Treatment of Opioid Addiction

1. Greater medication cost
2. Lower level of physical dependence (i.e., patients can discontinue treatment)
3. Not detectable in most urine toxicology screenings

There are definitely disadvantages to the medication, as well:

- Buprenorphine is more costly than methadone: According to the manufacturer, Suboxone® (16 mg/day) costs \$287.50 for a month's supply, compared to less than \$30 for a month's supply of methadone at usual doses.
- Overall, the medication causes a lower level of physical dependence. While this is generally seen as an advantage of the medication, it does make it easier for patients to discontinue treatment and return to use.
- Buprenorphine is not detectable in most urine tests, making monitoring for compliance difficult. However, this could also be an advantage of buprenorphine (for people who are randomly drug tested in the workplace).

## Clinical Case Studies Involving Buprenorphine

- Buprenorphine is equally effective as moderate (60 mg per day) doses of methadone.
- It is unclear if buprenorphine can be as effective as higher doses of methadone.
- Buprenorphine is as effective as moderate doses of LAAM.

Buprenorphine is equally effective as moderate doses of methadone (such as 60 mg per day) on primary outcome measures.

It is unclear if buprenorphine can be as effective as higher doses of methadone (such as 80 mg per day to more than 100 mg per day).

Buprenorphine appears to be equally effective as moderate doses of LAAM (such as 70 mg/70 mg/85 mg on a Monday/ Wednesday/Friday schedule).

## Clinical Case Studies Involving Buprenorphine

- Buprenorphine is mildly reinforcing, encouraging good patient compliance.
- After a year of buprenorphine plus counseling, as many as 75 percent have been retained in treatment compared to none in a placebo plus counseling condition.

Buprenorphine has a ceiling effect for the intense rush experienced with full agonists. \* However, patients do experience it as mildly reinforcing, thereby encouraging them to adhere to their dosing regimen.

Studies have shown that buprenorphine holds people in treatment much more effectively than counseling alone.

*\*Remember:*

• *Increasing the dose of a full agonist produces increasing effects until the receptor is fully activated and a maximum effect is reached.*

• *Partial Agonists share some characteristics of full agonists. At low doses, full and partial agonists produce effects that are essentially indistinguishable. However, increasing the dose of a partial agonist DOES NOT produce as great an effect as occurs with a full agonist. There is a **CEILING** to the agonist (intoxicating/euphoric) effects.*

## Buprenorphine/Naloxone: What You Need to know

- Basic pharmacology, pharmacokinetics, and efficacy is the **same** as buprenorphine alone.
- Partial opioid agonist; ceiling effect at higher doses
- Blocks effects of other agonists
- Binds strongly to opioid receptor, long acting

- The effect of the combination tablet is virtually identical to the buprenorphine-only product when taken sublingually.
- Both formulations demonstrate the ceiling effect at higher doses.
- Both formulations prevent the intoxicating effects if someone decides to also use another opioid.
- They are long-acting because of the high receptor affinity.

# Summary

- Use of medications as a component of treatment can be an important in helping the person to achieve their treatment goals.
- Opioid addiction affects a large number of people, yet many people do not seek treatment or treatment is not available when they do.
- Expanding treatment options can
  - make treatment more attractive to people;
  - expand access; and
  - reduce stigma.
- Opioids attach to receptors in the brain, causing pleasure. After repeated opioid use, the brain becomes altered, leading to tolerance and withdrawal.
- Medications operating through the opioid receptors, such as buprenorphine, prevent withdrawal symptoms and help the person function normally.