


**BUPRENORPHINE  
TREATMENT**

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

A Pharmacology Course  
Developed by Mountain West ATTC



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● The ATTC National Office developed and contributed the Buprenorphine Bibliography.

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



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## 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

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



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## 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.

A colorful illustration of a diverse group of people of various ages and ethnicities, some appearing to be in conversation or a social setting.

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## 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.

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## Treatment Admissions for Opioid Addiction

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## 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.

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## 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.

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## 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.

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## Four Reasons for Not Entering Opioid Treatment

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

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## 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.

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## Buprenorphine: An Exciting New Option

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## 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

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## 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.

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## 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)

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## 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

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## 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

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## Review of Opioid Pharmacology

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## 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.

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## 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

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

Agonist                      Morphine-like effect (e.g., heroin)

Partial Agonist            Maximum effect is less than a full agonist (e.g., buprenorphine)

Antagonist                    No effect in absence of an opiate or opiate dependence (e.g., naloxone)

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## Opioid Agonists

● Natural derivatives of opium poppy

- Opium
- Morphine
- Codeine

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# Opium



SOURCE: www.streetdrugs.org

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# Morphine



SOURCE: www.streetdrugs.org

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# Opioid Agonists

🌐 Semisynthetics: Derived from chemicals in opium

- Diacetylmorphine – Heroin
- Hydromorphone – Dilaudid®
- Oxycodone – Percodan®, Percocet®
- Hydrocodone – Vicodin®

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## Opioid Agonists

### ● Synthetics

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

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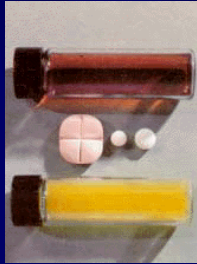
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## Methadone



## Darvocet



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

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## Opioid Partial Agonists

- Buprenorphine – Buprenex®, Suboxone®, Subutex®
- Pentazocine – Talwin®

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## Buprenorphine/Naloxone combination and Buprenorphine Alone



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## Opioid Antagonists

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



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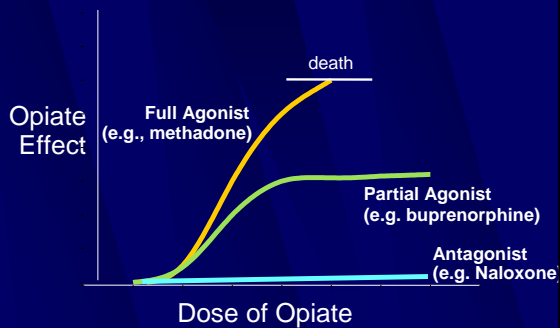
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## Partial vs. Full Opioid Agonist



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# Opioids and the Brain

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## Opioid Addiction and the Brain



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

Repeated opioid use → **Tolerance**

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

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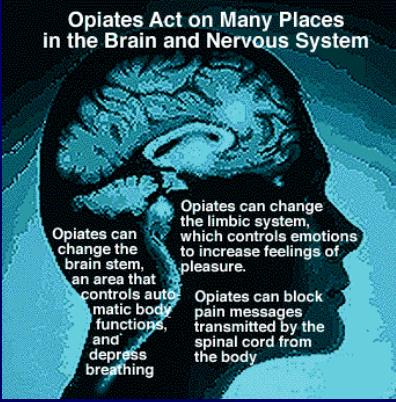
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### Opiates Act on Many Places in the Brain and Nervous System



Opiates can change the brain stem, an area that controls automatic body functions, and depress breathing

Opiates can change the limbic system, which controls emotions to increase feelings of pleasure.

Opiates can block pain messages transmitted by the spinal cord from the body

SOURCE: National Institute on Drug Abuse, [www.nida.nih.gov](http://www.nida.nih.gov).

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## 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

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## 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

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## 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

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## 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

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## 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

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## 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

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## 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

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## Treatment of Opioid Addiction

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## 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

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### 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

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### 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

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### 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.

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## 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.

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## 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

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## 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.

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