Module II

Opioids 101

Module II: Opioids 101

Module II is designed to introduce trainees to basic facts about opioids, including information on pharmacology, acute and long-term effects, and basic information about treatments for opioid addiction. This module contains background information necessary to understand the role of buprenorphine in the opioid treatment system. If the audience is already highly knowledgeable about opioid treatment, this module should be abbreviated or omitted.

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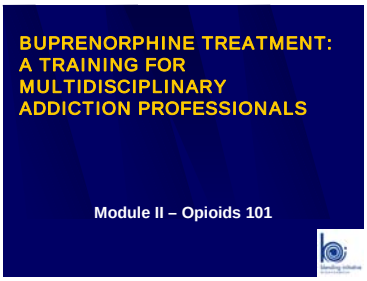
<td> 
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<td>Slide 1: Title Slide
The next module provides an overview of opioids and opioid treatment, setting the stage to see the role of buprenorphine in the treatment system.</td>
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<td>Slide 2: Ritual of a Heroin User

Read quote aloud OR have a trainee read the quote. Then, invite a few trainees to share their reactions to the quote.</td>
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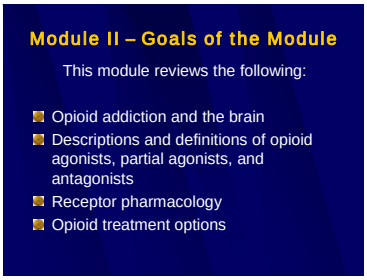
<td> 
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<td>Slide 3: Module II – Goals of the Module

We are now going to turn a little more directly to the issue of opioid addiction. In this module, we will discuss the impact of opioids on the brain, make sure that everyone is aware of and able to define all of the classes of opioids, look at how opioids work, and finally look at treatment options for opioid users.</td>
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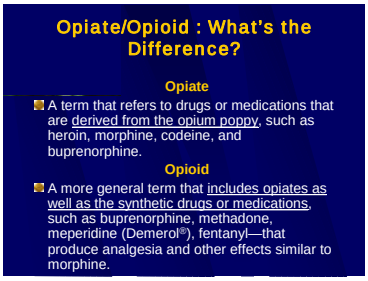
<td> 
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<td>Slide 4: Opiate/Opioid: What's the Difference?
Throughout this training we are using the term opioid to define the class of drug with which we are dealing. It is important to understand what this term means.
• Opiate refers only to drugs 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.</td>
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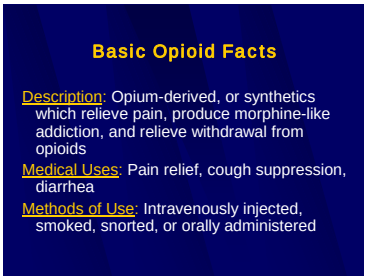
<td> 
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<td>Slide 5: Basic Opioid Facts
Description: All opioids work basically the same way, regardless of their derivation.

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.</td>
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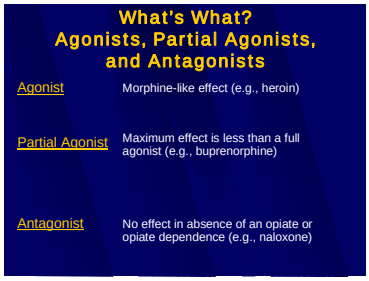

Slide 6: What's What? Agonists, Partial Agonists, and Antagonists

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.

Slide 7: Opioid Agonists

Natural Derivatives

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

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<td>Slide 8: Opium

Show picture for a few seconds and then move on.</td>
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<td>Slide 9: Morphine

Show picture for a few seconds and then move on.</td>
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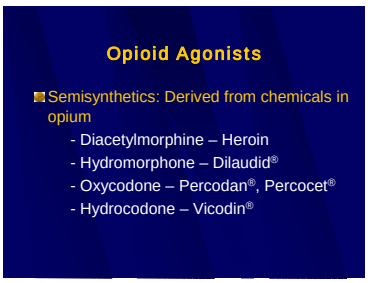
<td> 
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<td>Slide 10: Opioid Agonists

<u>Semisynthetics</u>
These substances are derived from chemicals extracted from the opium poppy. They also fall into both the opiate and opioid categories.</td>
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<td>Slide 11: Heroin

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</td>
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<td>Slide 12: Bayer Graphic

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.

Note: In larger rooms the text of this slide is difficult to read and should therefore be read aloud.</td>
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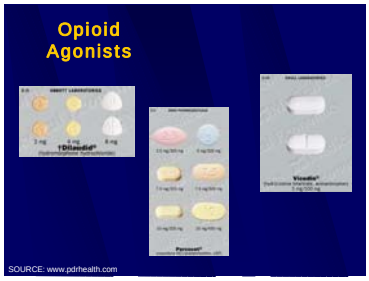


Slide 13: Opioid Agonists

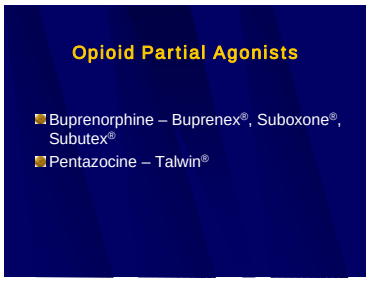
Show picture for a few seconds and then move on.

Slide 14: Opioid Agonists

<u>Synthetics</u>
These substances are synthetically manufactured. They are considered opioids, but are NOT opiates.

Slide 15: Methadone/Darvocet

Show picture for a few seconds and then move on.



Slide 16: Opioid Partial Agonists
Buprenex® 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® is the buprenorphine/naloxone combination tablet and Subutex® is the buprenorphine-only tablet. Only these two tablet formulations are approved for the treatment of opioid addiction.

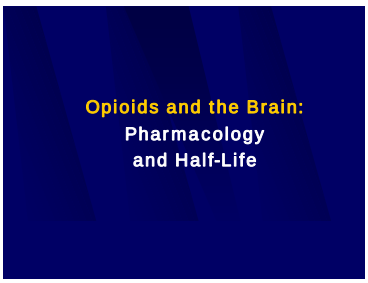
Pentazocine (Talwin®) is marketed for pain; it **IS NOT** approved for the treatment of opioid addiction.

Slide 17: Buprenorphine/Naloxone Combination and Buprenorphine Alone

This is what the two sublingual buprenorphine tablets look like.

Slide 18: Opioid Antagonists

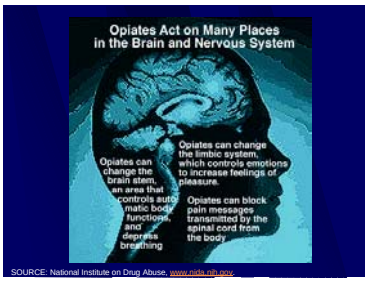
As was previously stated, antagonists are those substances that block the affects of opioid agonists. Two examples are naloxone (the same medication in the buprenorphine/naloxone combination tablet) and naltrexone.



Transition

Slide 19: Opioids and the Brain: Pharmacology and Half-Life

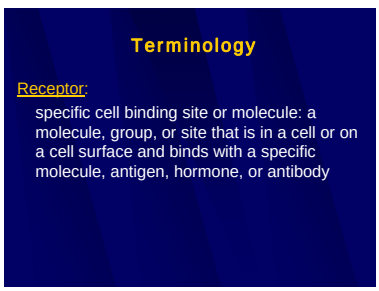
So now that you know which drugs and medications are included in the class known as opioids, let's look at how they work.



Slide 20: NIDA Brain Graphic

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.



Slide 21: Receptor Pharmacology: Terminology

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

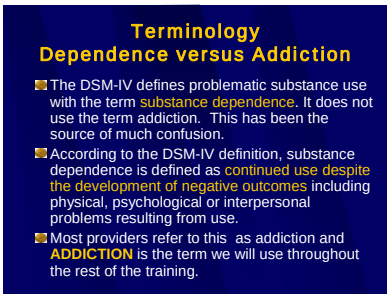
Receptor

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.

****SMALL GROUP EXERCISE****

Slide 22: Dependence vs. Addiction: What's the Difference?

Break the audience into small groups (3-4 people), and ask them to discuss the difference between dependence and addiction. After approximately 10 minutes, have the group reconvene and ask for a few volunteers to describe their discussions.

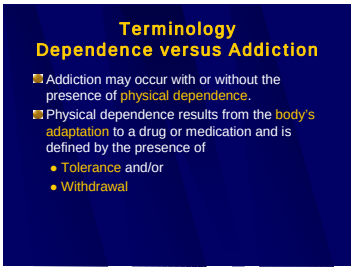


Slide 23: Dependence versus Addiction

The standard for understanding all mental health disorders (including substance abuse) is the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). However, because the DSM uses the term "dependence" to mean two different things, a great deal of confusion has arisen.

The DSM defines "substance dependence" as continued use in spite of a pattern of negative physical, psychological and interpersonal outcomes resulting from use.

Most providers use the term "addiction" to describe this pattern of problems. In order to keep this term distinct, we will use the term **addiction** *(rather than dependence)* throughout this training to refer to this pattern of problems resulting from use.



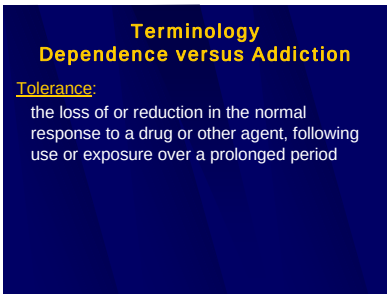
Slide 24: Dependence versus Addiction

The other use of the term "dependence" is to describe the body's reaction to the presence of an addictive substance—that is physical dependence on the substance.

Physical dependence is one symptom of addiction, but it is important to remember that addiction can occur with or without physical dependence.

Physical dependence is defined by the presents of tolerance and/or withdrawal.

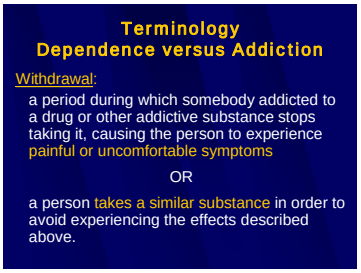
Let's look at the specific definitions of these terms.



Slide 25: Dependence versus Addiction

Tolerance

Tolerance deals with the body's adaptation to a drug or medication. With repeated exposure, the response to the substance lessens. It therefore requires a higher dose to get the same effect.



Slide 26: Dependence versus Addiction

Withdrawal

This is another indicator of the body's adaptation to the drug. This process occurs when the normal dose is reduced or stopped and the person experiences painful or uncomfortable symptoms OR the person uses a similar substance in order to avoid these painful feelings.

Let's look at the problems that the DSM-IV identifies:

Slide 27: DSM-IV Criteria for Substance Dependence

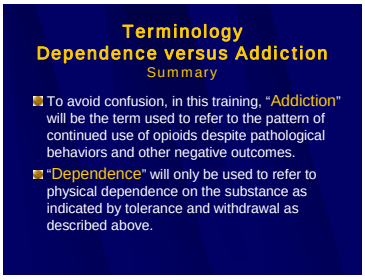
According to the DSM-IV, substance use disorders occur on a continuum. The less sever form of the problem is called abuse and is defined as having repeated problems associated with use, but generally the individual is still at least somewhat functional in their lives. As the problem worsens, the person moves on to addiction (or what the DSM-IV calls substance dependence) in which functioning is markedly impaired.

Addiction is based on clusters of behaviors and physical effects. It is defined as a "maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by three (or more) of seven symptoms occurring at any time during a 12-month period."

Read the bullets aloud.

Additional points to mention:

Bullet #3: "*taking larger amounts*" – indicates a loss of control over moderating your drug use. "*Over time*" can also be stated as "*longer periods than intended.*"

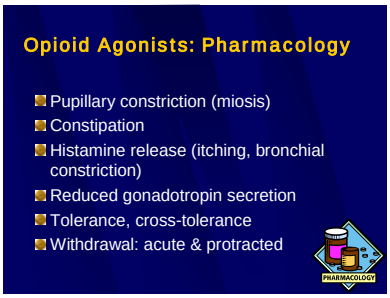


Slide 28: Dependence versus Addiction (summary)
For clarity, let's review the terms again:

Read slide aloud.

Slide 29: Opioid Agonists: Pharmacology
So how do opioids work?

Opioids work by stimulating the opioid receptors in the brain and GI tract. When they bind to the receptor, users experience relief from pain, cough suppression, feelings of euphoria, and they may become stuperous. If the dose is high enough, they may experience a slowing of respiration. This final symptom can lead to death.



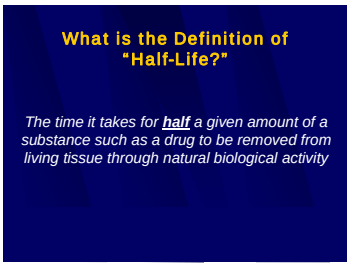
Slide 30: Opioid Agonists: Pharmacology

Other side effects of opioids include:

- Constriction of the pupils so that they become very small (sometimes referred to as pinpoint pupils);
- Constipation;
- An allergic type reaction accompanied by itching and/or difficulty breathing; and
- Lower libido due to decreases in sex hormones.

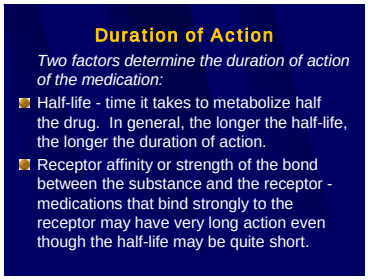
We have already discussed the definition of tolerance. With opioids, you also see cross-tolerance. This means that once tolerance develops for one substance (e.g., heroin) you will see tolerance for other opioids, as well (e.g., codeine or Demerol). If the person is receiving treatment with an opioid medication (either as a treatment for opioid addiction or for other medical indications), the dose will need to be adjusted depending upon the level of tolerance.

In a person who is otherwise generally healthy, withdrawal from an opioid agonist is not life threatening. However, it is characterized by drug cravings and marked distress, including flu-like symptoms, joint pain, and anxiety. It is also frequently associated with relapse to drug use. Once the immediate withdrawal from the drug is over (usually after a few days), there are residual emotional and physical symptoms that place the patient at significant risk for relapse.



Slide 31: What is the Definition of "Half-Life?"

Read the definition aloud.



Slide 32: Duration of Action

Duration of action is the length of time that a person experiences the effects of the drug. Two factors determine the duration of action:

- Half-life: The slower the medication is removed from the body, the longer the experience lasts. Usually the next dose of a medication is taken at about one half-life.

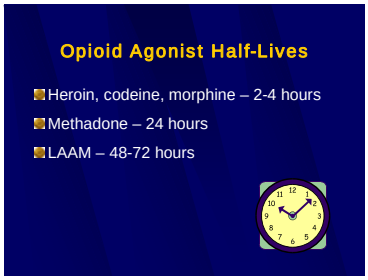
- Affinity: The strength with which a drug binds to a receptor. A medication that has high receptor affinity stays on the receptor for a longer period of time, and therefore continues to activate the receptor. This results in a longer duration of action than medications or drugs with lower affinity.

A faster route of administration (such as smoking or injection), a shorter half-life, and a faster onset of action are all associated with a higher abuse potential for a drug.

Slide 33: Opioid Antagonist Half-Lives

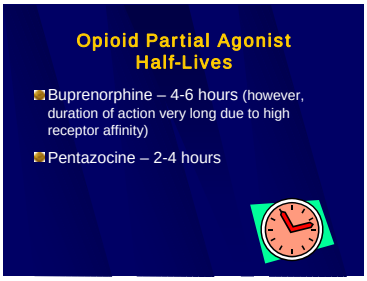
Naloxone is a very fast-acting drug that is metabolized very quickly. This makes the medication very appropriate for treating emergency conditions (e.g., overdose).

Naltrexone, however, is much longer acting, making it a better choice for antagonist maintenance therapy.



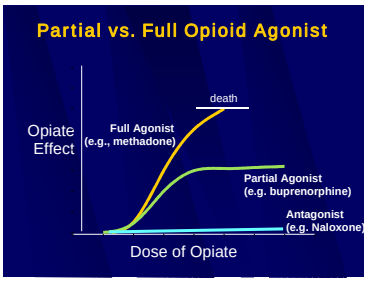
Slide 34: Opioid Agonist Half-Lives

One reason people feel more stable on methadone than on heroin is because the medication has a very long half-life. The person feels stable taking the medication only once per day, as opposed to needing to dose every few hours on heroin.



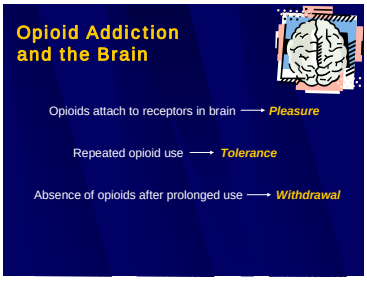
Slide 35: Opioid Partial Agonist Half-Lives

Unlike methadone, buprenorphine has a fairly short half-life. However, it still has a very long duration of action. In this case, the duration of action results from high receptor affinity.



Slide 36: 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.



Slide 37: Opioid Addiction and the Brain

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).

Mention that craving/triggers will be discussed in greater detail in Module VI.

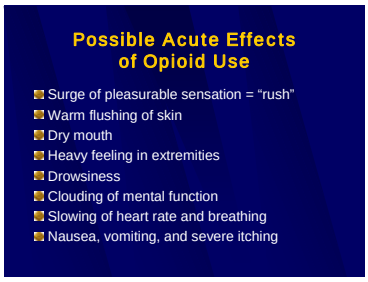
Slide 38: What Happens When You Use Opioids?

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.

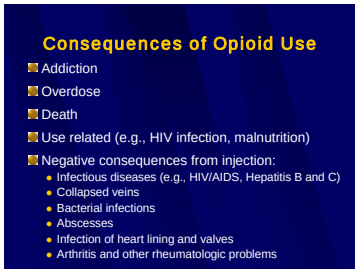


Slide 39: Possible Acute Effects of Opioid Use

Summarize the symptoms associated with acute effects, chronic use, and withdrawal.

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."



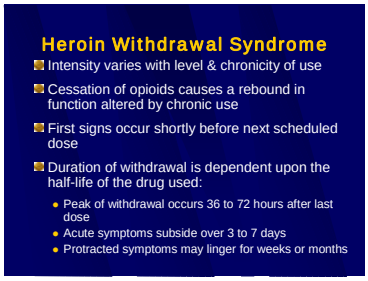
Slide 40: Consequences of Opioid Use

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 form unprotected sexual behaviors, malnutrition, etc.

Many of the consequences refer specifically to injection drug use:

- Collapsed veins resulting from repeated injections.
  Ask trainees: What do people do if their veins collapse? *(Answer: find another place).*

  Ask trainees: 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.



Slide 41: Heroin Withdrawal Syndrome

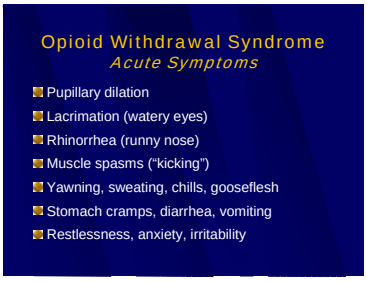
Once the body becomes accustomed to the drug being on board, it may react if the drug is removed. The intensity of the withdrawal symptoms will depend on the level of use (dose and type of opioid) and the frequency and duration of use (chronicity).

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.



Slide 42: Opioid Withdrawal Syndrome: *Acute Symptoms*

Acute withdrawal symptoms are the opposite of acute intoxication symptoms.

Summarize the acute withdrawal symptoms.

Slide 43: Opioid Withdrawal Syndrome: *Protracted Symptoms*

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

Summarize the acute withdrawal symptoms.

Anorgasmia = inability to have an orgasm
Anhedonia = overall lack of pleasure (everything is gray)

Transition

Slide 44: 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. The next section of the training will look at the treatment options available for opioid addiction.

Slide 45: Treatment Options for Opioid-Addicted Individuals

The successful treatment for opioid addiction requires both management of physical withdrawal symptoms and behavioral and cognitive changes that encourage the patient to abstain from using the drug of abuse in the future. Providing psychosocial and counseling services along with pharmaceutical treatment increases the likelihood of achieving long-term, comprehensive lifestyle changes and preventing relapse. You want to help the patient restore a degree of normalcy to brain function and behavior, thereby leading to increased employment rates, reduced criminal behavior, and lowered risk of HIV, hepatitis C, and other diseases.

Stress the importance of combining both treatment approaches (Bullet #3).

The bottom line is that you need to tailor the treatment to meet the particular needs of the patient (e.g., deciding between inpatient and outpatient, behavioral and pharmacological, etc.).

Slide 46: How Can You Treat Opioid Addiction?
Medically-Assisted Withdrawal

The individual is systematically withdrawn from addicting drugs. Medications (e.g., methadone, buprenorphine, clonidine) are used to alleviate withdrawal symptoms while the person gradually returns to an opioid-free state.

It can be done successfully in inpatient or outpatient settings, but the treatment plan should be carefully developed to ensure adequate structure and support.

Generally, a medical provider supervises the withdrawal to monitor medical safety and administer medications to relieve discomfort.

Generally, this approach is not sufficient by itself to transition someone to maintaining an ongoing opioid-free life. Longer-term treatment that helps the person to develop new behaviors and strategies for coping is critical.

Patients who are not successful in withdrawing or who choose not to withdraw from opioids should be considered for treatment with medications as part of the treatment plan (either short- or long-term).

Slide 47: How Can You Treat Opioid Addiction?
Long-Term Residential Treatment

Provides a highly structured environment (away from the person's usual environment) in which treatment occurs.

Residential treatment may employ a variety of models, including Therapeutic Communities and cognitive behavioral therapy.

TCs focus on the resocialization of the individual and use the program's entire community, including other residents, staff, and the social context, as active components of treatment.

Slide 48: How Can You Treat Opioid Addiction?
Outpatient Psychosocial Treatment

People involved in outpatient psychosocial treatment continue to live in the community while receiving their treatment.

The exact structure and elements of treatment vary greatly from program to program.

Generally, outpatient treatment is less costly than residential treatment.

Outpatient programs also offer increased flexibility, allowing people to continue to hold down jobs and make use of social supports in the community.

Slide 49: How Can You Treat Opioid Addiction?
Outpatient Psychosocial Treatment

Group counseling is generally the primary treatment in these programs.

Medically assisted withdrawal is generally done using clonidine and other non-narcotic medications.

People often report being very uncomfortable during the withdrawal process.

For this reason, many people leave treatment prematurely because they cannot tolerate the symptoms.

Slide 50: How Can You Treat Opioid Addiction?
Behavioral Therapies

Behavioral therapies are designed to help individuals change their thought patterns around drug use and learn new behaviors to help them stop using and avoid relapse.

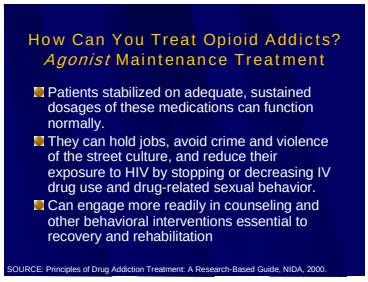
Two general strategies have shown a great deal of promise:
Contingency management:
- Helps the patient to adopt new behaviors by reinforcing behaviors that move them toward their treatment goals

Cognitive-behavioral interventions:
- Help the patient to change the way they think and behave with regards to drug use
- Increase positive coping strategies

Many different types of behavioral therapies have been used successfully for substance abuse disorders. These include:
- Motivational Enhancement Therapy
- The Matrix Model
- Cognitive and Cognitive-Behavioral Therapy
- Community Reinforcement Approach
- Self-Help Programs

*MENTION THE FOLLOWING **FREE** RESOURCES:*
SAMHSA's *Treatment Improvement Protocol* (TIP) series includes a number of documents that contain best-practice guidelines for the provision of interventions and therapies for individuals with substance abuse disorders.

The *Principles of Drug Addiction Treatment: A Research-Based Guide* (a.k.a., the NIDA Blue Book) reviews treatment approaches that have empirical support for their efficacy.



Slide 51: How Can You Treat Opioid Addiction?
Agonist Maintenance Treatment

Agonist maintenance helps to stabilize people so that they don't constantly experience the cycles of use and withdrawal. This allows them to function more normally.

The negative behaviors associated with use are diminished.

The person can immediately engage in the treatment experience while interested and motivated to receive treatment, rather than feeling sick (withdrawal) for a week or more and then beginning the treatment process.

Slide 52: How Can You Treat Opioid Addiction?
Agonist Maintenance Treatment

These treatments have been conducted primarily on an outpatient basis in specific opioid treatment programs. With the addition of buprenorphine to the treatment system, patients can also receive treatment through physicians in the offices.

Generally, a long-acting opioid (traditionally methadone, now also buprenorphine) is used. These medications prevent the occurrence of withdrawal symptoms and block the effects of illicit opioids if they are used. They also help to decrease craving for the drug.

Slide 53: How Can You Treat Opioid Addiction?
Agonist Maintenance Treatment

Maintenance programs are most effective if they are combined with an effective behavioral treatment program.

Additionally, patients may need treatment for other medical or psychological conditions. They may also need a variety of social support services. Social services include:

- Vocational rehabilitation
- Employment
- Education
- Housing
- Case management
- Parenting
- Socialization skills
- Anger management

Slide 54: Benefits of Methadone Maintenance Therapy

Review and summarize bullet points.

Slide 55: How Can You Treat Opioid Addiction?
Antagonist Maintenance Treatment

Use of opioid antagonists can also be effective. As with agonist treatment, antagonist treatment is generally conducted through an outpatient setting.

The antagonist is prescribed after medical withdrawal from opioids is complete.

If antagonists are administered before complete withdrawal, the person may experience immediate and intense withdrawal.

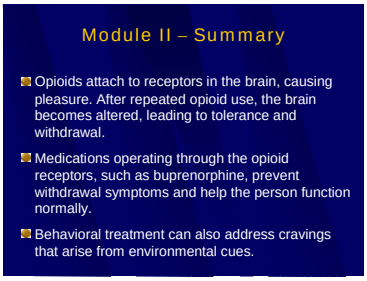
Slide 56: How Can You Treat Opioid Addiction?
Antagonist Maintenance Treatment

Antagonists block the effects of any illicit opioid. Over time, this helps the person to break the pattern and desire of use.

One problem with antagonist treatment is that patients stop taking them because they want to get the experience of taking an agonist.

Effective antagonist maintenance therefore requires:

- A positive therapeutic relationship with the treatment provider;
- Ongoing counseling; and
- Monitoring of medication to determine level of compliance.



Slide 57: Module II – Summary

Review and summarize bullet points.