

Managing Opioid Abuse, Dependence, and Addiction in a Primary Care Setting

Jean J. Bonhomme M.D., M.P.H.
Assistant Professor,
Department of Psychiatry
Morehouse School of Medicine
jbonhomme@msm.edu



Opiates / Opioids

- **Opioids** have morphine-like actions.
- **Natural** opiates are alkaloids found in the resin of the opium poppy e.g.:
 - morphine,
 - codeine and
 - thebaine.



Opiates / Opioids

- **Semi-synthetic** opiates are chemically altered derivatives of natural opioids, e.g.:
 - hydromorphone,
 - hydrocodone,
 - oxycodone,
 - oxymorphone,
 - diacetylmorphine (heroin)



Opiates / Opioids

- Fully synthetic opioids are artificial compounds with opioid activity, e.g.:
 - fentanyl,
 - methadone,
 - tramadol (ultram), and
 - propoxyphene (darvon).

Opiates / Opioids

- Endogenous opioid peptides are substances produced naturally by the body, e.g.: endorphins, enkephalins, and dynorphins.
- Morphine is “Endorphin’s evil twin”



An endorphin is a natural brain signal that helps us feel good.



Morphine, a chemical imposter, affects the emotional state by mimicking the brain's natural endorphins.



Key Neurotransmitter Functions

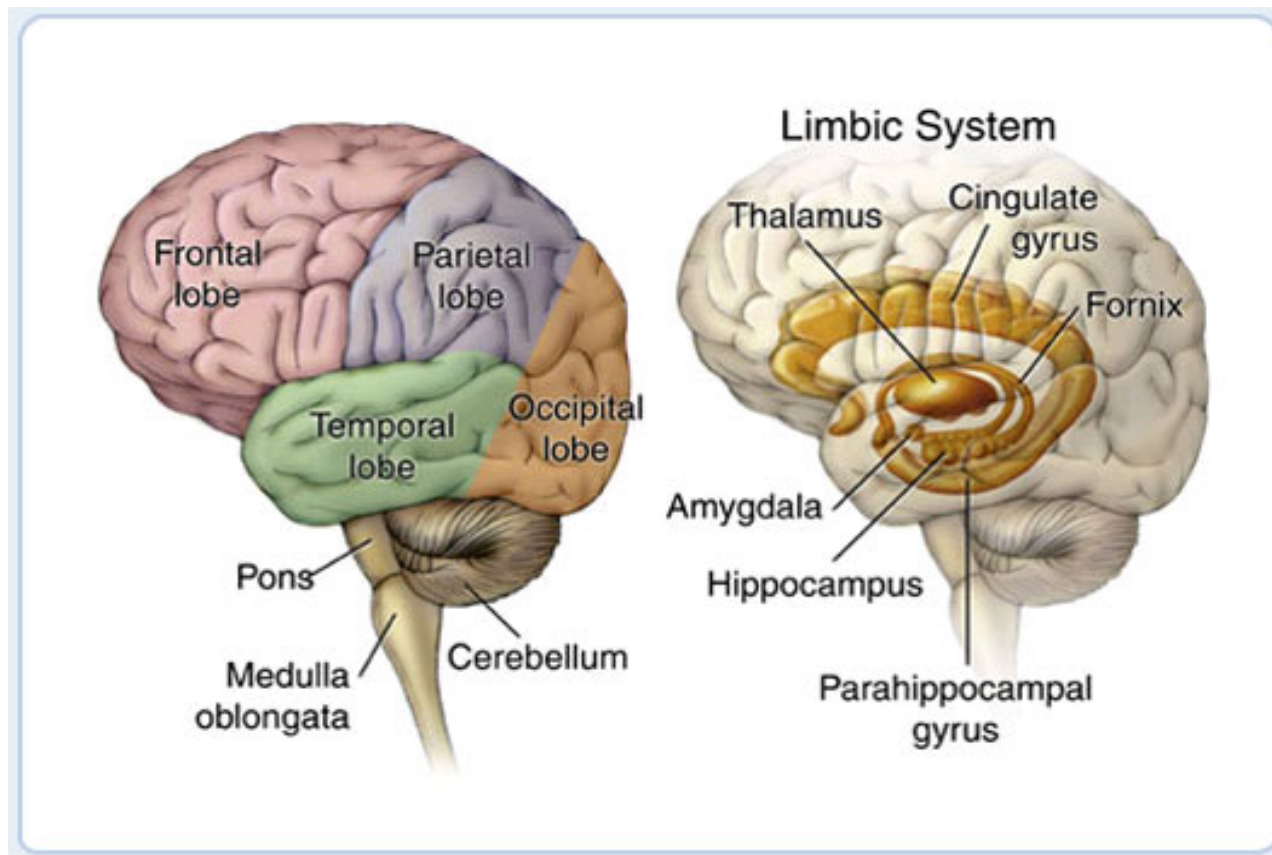
- Acetylcholine (Ach): thought, movement
- Dopamine (DA): pleasure, motion
- Serotonin: relaxation, mood
- Glutamate: the brain's accelerator pedal
- Gamma-amino-butyric acid (GABA): the brain's brake pedal
- **Endorphins (Enkephalins, Dynorphins): the brain's natural painkillers**



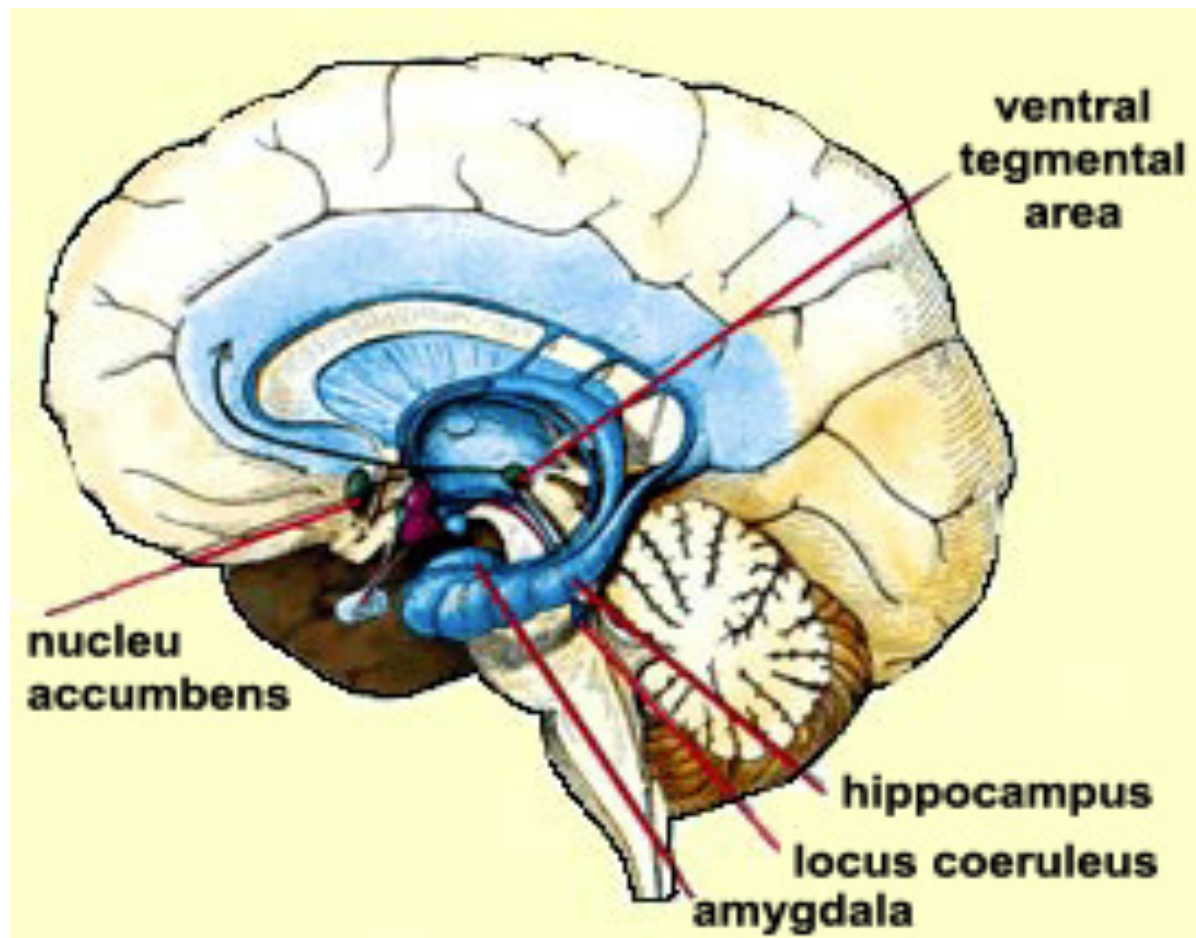
Opiates / Opioids

- Opioids bind to opiate receptors concentrated in specific areas within the reward pathway (including the VTA, nucleus accumbens, and cortex).
- Opioids also bind to areas involved in the pain pathway (including the thalamus, brainstem, and spinal cord).
- Binding of opioids to areas in the pain pathway produces analgesia (decreased perception of pain).

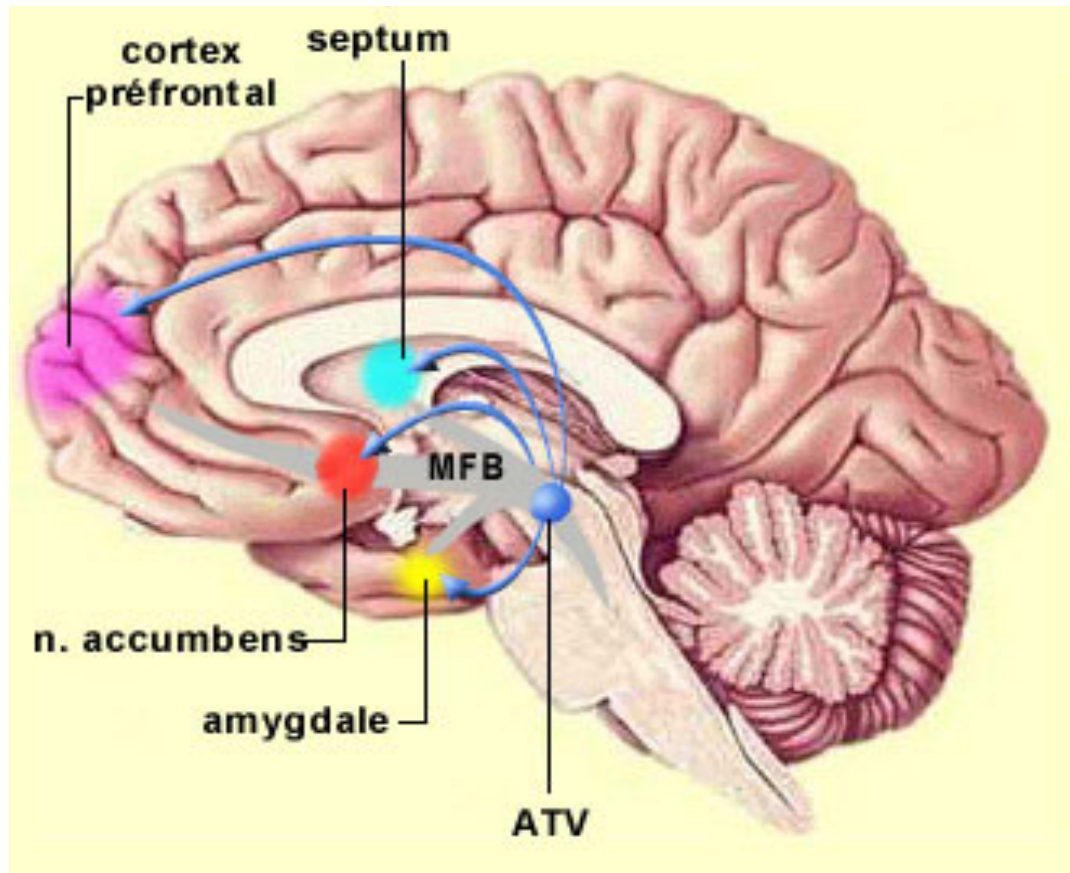
Brain Areas In Dependence: Brainstem and Thalamus



Brain Areas In Addiction: N. Accumbens and VTA



Brain Areas In Addiction: Prefrontal Cortex





Opiates / Opioids

- Brain regions mediating the development of opiate or opioid **dependence** involve specific areas **separate** from the reward pathway, the thalamus and the brainstem.
- The parts of the reward pathway involved in opiate or opioid addiction were shown for comparison.
- Many of the withdrawal symptoms from heroin or morphine are generated when the opiate receptors in the thalamus and brainstem are deprived of morphine.



Addiction Defined

- **Addiction** is defined as *continued substance use in the face of adverse consequences*.
- Extreme *compulsion* is the overriding feature.
- Examples - Using drugs and/or alcohol to the point of intoxication and grossly impaired function, e.g. a person gets arrested for drunken driving and their license is confiscated.
- Two days later they are on the road again and drunk. Punishment appears to be no deterrent.
- **Key:** In the presence of the substance, function *deteriorates*, but use *continues*.



Dependence Defined

- **Dependence** is very different - defined as a state in which the body *relies* on a substance for normal functioning.
- Example: A person has a ruptured disk in the lower back, with pain is so severe that they cannot work or take care of their children.
- When they are given an opiate pain medication, the pain is reduced to the point where they can function normally and responsibly.
- **Key:** In the presence of the substance, function *normalizes*.



What is the Importance of This Distinction?

- DSM-IV does not make any distinction here.
- Usually neither do the criminal courts.
- In both instances, the person really needs the substance, but the ***consequences*** of their use are completely different.
- Not making this distinction lumps persons with a legitimate need for a controlled substance together with those who are actively misusing them.
- A crucial distinction: between people who are being helped and those who are harming themselves and others by their drug use.
- Example – Sickle Cell patient in ER.



The Anatomy Underlying This Distinction

- Addiction is clearly a brain disease.
- Different parts of the brain are responsible for addiction (versus dependence) to opiates.
 - The areas in the brain underlying addiction to opioids are the reward pathway (including the VTA, nucleus accumbens, and prefrontal cortex).
 - **All** drugs of addiction appear to involve the reward pathway.
 - Those areas underlying dependence to morphine are the thalamus and brainstem.



Dependence Explained

- **It is possible to be dependent without being addicted, a very important distinction.**
- Even those who need very high doses of medication may not be addicted.
- Most people treated with opiates in a hospital setting for pain control after surgery are unlikely to become addicted. There is usually no pattern of compulsive use and prescribed use is short-lived.
- However, if one is addicted, they are most likely dependent as well (withdrawal, detox issues).



Why Did DSM-IV Fail to Make This Distinction?

- There was some debate as to whether compulsive substance use leading to adverse consequences should be called “addiction” or “dependence.”
- It was felt by some that the term “addiction” was too pejorative and prejudicial, such that persons with a diagnosis of addiction would be very harshly judged.
- The term “dependence” was felt to be much less prejudicial, so by one vote, it was decided to use the term “dependence.”
- This has led to much confusion. Plans exist currently to change terminology for DSM-V.



So How Do We Define Substance *Abuse*?

- In drug ***abuse***, function may deteriorate in the presence of the drug and other adverse consequences may ensue, but there is no ***compulsion*** to continue using the drug.
- Example: A person uses a drug for recreational purposes for some time, then has a bad experience, such as an overdose or a brush with the law. They say “That’s it – I’m through with this stuff.”
- This is not addiction, because they voluntarily left it alone when it clearly became more trouble than it’s worth.
- A true addict cannot do this.



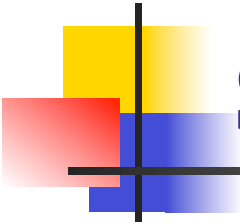
Tolerance Explained

- Tolerance is defined as progressively decreasing response to a drug with exposure. Increased doses are necessary to get the same effect.
 - This usually refers to repeated or prolonged exposure, which is called **chronic tolerance**.
 - Rarely, sensitivity to a drug may increase with repeated exposure, called **reverse tolerance**.
 - **Having high tolerance, e.g. needing high doses of a drug is NOT addiction.**



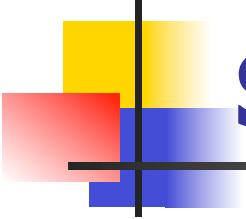
The Withdrawal Syndrome Explained

- Withdrawal is a group of negative physical and mental effects resulting from discontinuation of substances by persons who have become habituated to their use.
- Withdrawal symptoms may include severe drug cravings as well as a group of negative physical symptoms that may occur when a person suddenly stops using a drug to which he or she has become dependent.
- Generally, the longer the drugs are taken and the higher the dose, the more severe the symptoms.



Opioid Withdrawal: Signs and Symptoms

- yawning,
- sweating,
- lacrimation,
- rhinorrhea,
- anxiety,
- restlessness,
- insomnia,
- dilated pupils,



Opioid Withdrawal: Signs and Symptoms

- piloerection,
- chills
- tachycardia,
- hypertension,
- nausea/vomiting,
- crampy abdominal pains,
- diarrhea, and
- muscle aches and pains.



The Withdrawal Syndrome Does NOT Equal Addiction

- If you give adequate doses of opiates to a person in opiate withdrawal, often they can resume normal function. After being gradually tapered off, most people do not go back to using.
- By contrast, truly addicted people who have been incarcerated for years and are long past any remnant of the physical withdrawal syndrome may relapse on drugs within months, weeks, days or even hours of their release.



Route of Drug Administration and Risk of Addiction

- Smoking is actually potentially the most addictive route of drug administration.
- Behavioral science has proven that the faster a reward or punishment follows an action, the greater the impact of that reward or punishment on future behavior.
- When a drug is smoked, it takes a short circulatory path, into the lungs, into the left side of the heart, and into the carotid arteries to the brain.



Route of Administration and Addiction Potential

- Because of the enormous surface area of the lungs (roughly the area of a tennis court), high blood levels of the drug are commonly attained, as is the case with injection.
- This process takes only about **seven** seconds. Rapidity of onset of action is strongly associated with addictive potential.
- Just like training a dog with food rewards, if the reward follows quickly, the behavior is better reinforced.



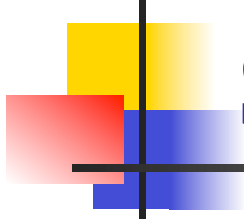
Route of Administration: Bypassing Needle Aversion

- Consider how hard it is to give up cigarettes, cocaine addiction grew explosively when the smokeable crack form was introduced.
- Smoking is much more socially acceptable behavior than using needles or snorting due to our history of accepting tobacco smoking.
- Prescription pain pill use also made recreational opioid use more acceptable.
- Danger sign: when a drug is presented in smokeable or pill form, a major social barrier to initiating its use (called needle aversion) is removed.



Pharmacological Half-Life and Addiction

- Methadone treatment, which only needs to be taken once daily to suppress withdrawal is much less likely to promote constant drug seeking behavior than oxycodone or heroin, which must be taken several times daily to maintain adequate blood levels.
- People addicted to heroin are practicing drug seeking / using behavior several times a day, every day, day and night.
- People on methadone take one dose in the morning and go about their business for the rest of the day.



The Demographics of Substance Use Disorders

- The National Survey on Drug Use and Health
- **<http://www.oas.samhsa.gov/nhsda.htm>**
- An annual survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA)
- Estimates the prevalence of illicit drug use in the United States.
- Some of the more notable statistics from the 2004 study follow.



Nonmedical Use of Psychotherapeutic Medications

- In 2004, 6.0 million persons were current users of painkillers or psychotherapeutic drugs taken nonmedically (2.5% of the population).
- An estimated 180,000 used heroin.
- After about calendar year 2001, the illicit use of prescription pain pills began to surpass heroin, and now does so by a wide margin.
- These include 4.4 million who used pain relievers.



Mortality and Morbidity of Untreated Opiate Addiction

- Untreated heroin addicts suffer a death rate thirteen times that of the general population.
- More so today than ever, heroin is not the only opiate contributing to the landscape of addiction.
- Excess deaths and illnesses occur from a wide variety of causes, including but not limited to:
 - Drug effects, overdoses and interactions,
 - Intentional and unintentional injuries
 - Infectious diseases.



The economic costs of heroin addiction in the United States

- Mark T L; Woody et al (2001)
- We estimate that the cost of heroin addiction in the United States was \$21.9 billion in 1996.
 - Of these costs, productivity losses accounted for \$11.5 billion (53%), criminal activities \$5.2 billion (24%), medical care \$5.0 billion (23%), and social welfare \$0.1 billion (0.5%).
 - This economic burden highlights the importance of investment in prevention and treatment.



Is the Problem of Opiate Addiction Likely to Increase?

- Increasing purity of heroin has been reported in the Southeastern U.S. – up to 70% pure on the streets of Atlanta. Purity is catching up with the Northeastern U.S.
- Increasing availability of Pharmaceutical opiates – 12 year olds have ordered Oxy-contin from offshore sites via internet.
- Newer opiates – Oxy-Contin, Fentanyl, etc.
- Effective non-injection delivery systems – smoking, snorting, eating the contents of fentanyl patches.



Potential red flags for misuse of prescription opioids

- Medical history suggestive of “doctor shopping”
- Running out of medications repeatedly
- False claims of lost prescriptions
- Suspected theft of prescriptions/prescription pads
- Possession of numerous opioid medication bottles.



Potential red flags for misuse of prescription opioids

- Family members or the practitioner may notice:
 - unexplained changes in personality
 - marked mood swings, and
 - unusually pronounced drug side effects such as:
 - atypical drowsiness,
 - marked constipation or
 - confusion.



Potential red flags for misuse of prescription opioids

- Taking more medication than prescribed or more often than prescribed
- Signs of taking medications in an unusual way, such as unexplained needle marks or nasal problems possibly due to crushing and snorting pills
- Changes in social behaviors may include changes in networks of friends, declining grades, frequent disciplinary actions or abandonment of favored extracurricular activities in school, excessive absenteeism or failing job performance



Standardized measures of addiction severity

- Addiction Severity Index (ASI) - adapted to both alcohol (ASI-alc) and drug addiction (ASI-drug)
- Clinical Opiate Withdrawal Scale (COWS)
- Subjective Opiate Withdrawal Scale (SOWS)
- Drug Abuse Screening Test (DAST)
- Clinical Institute Narcotic Assessment Scale for Withdrawal Symptoms (CINA)
- CAGE-AID
- Narcotic Withdrawal Scale



Opioid Treatment Options and the Primary Care Practitioner

- Opioid addiction treatment with pharmacologically-active opioids remains controversial.
- The efficacy of methadone in reducing or eliminating heroin use has long been established, but methadone remains available principally in pain clinics and specialized dosing centers that may be geographically distant from users, especially users not residing in large cities.



Opioid Treatment Options and the Primary Care Practitioner

- Widespread availability of buprenorphine offers a distinct advantage over methadone.
- The Drug Addiction Treatment Act of 2000 permits physicians to treat up to thirty patients with buprenorphine in office-based settings.
- A DEA-licensed physician can obtain credentials to prescribe buprenorphine by taking a readily available 8-hour training program online or in class.



Opioid Treatment Options and the Primary Care Practitioner

- Initially, an office-based practitioner may be allowed to prescribe buprenorphine preparations to a maximum of thirty patients.
- However, after one year of practice permission may be obtained to increase the number of patients to 100 via physician request to SAMHSA.
- <http://buprenorphine.samhsa.gov/pls/bwns/training>



Opioid Treatment Options and the Primary Care Practitioner

- Buprenorphine also may be prescribed in the setting of a Methadone maintenance clinic, in which case the program may treat administration as similar to methadone with respect to:
 - observed ingestion,
 - random urine drug screens,
 - and earned take home medication.



Pros and Cons: Methadone and Buprenorphine

- Even at high doses, buprenorphine only partially activates the opioid mu receptor to approximately 40% of full output.
- In severely addicted patients, methadone, which activates the receptor fully, may be more efficacious therapeutically.
- High-dose methadone-treated subjects remain in treatment longer, exhibiting longer periods of abstinence and more drug-free UDS than buprenorphine patients.



Pros and Cons: Methadone and Buprenorphine

- Buprenorphine's partial mu agonist activity may induce a milder withdrawal syndrome than most opioids, thus discontinuing buprenorphine may be easier.
- However, a misconception exists that people who taper off buprenorphine can easily remain drug free thereafter.
- Like methadone, many patients who terminate treatment may not be able to sustain abstinence.



Pros and Cons: Methadone and Buprenorphine

- Studies on opioid-related mortality demonstrate that risk of death increases substantially in the first year after discontinuing either methadone or buprenorphine, principally from relapse consequences.
- High-dose buprenorphine has been shown to be more effective than low-dose methadone in client retention and illicit drug-free urine screen rates.



Pros and Cons: Methadone and Buprenorphine

- Buprenorphine is largely self-administered, causing concern about inadequate frequency of monitoring.
- Some clients may purposely decide to use buprenorphine intermittently.
- In methadone clinics, patients receive random UDS. Those entrusted with one to four weeks of medication are subject to being called back randomly for UDS and mg. counts on remaining medication.



Pros and Cons: Methadone and Buprenorphine

- Outpatient methadone treatment can be effective in treating dual opioid and cocaine dependence, especially when combined with other behavioral and pharmacological interventions aimed at achieving sustained cocaine abstinence.
- Buprenorphine appears less effective than methadone in reducing or eliminating co-occurring opioid and cocaine dependence.



Pros and Cons: Methadone and Buprenorphine

- A meta-analysis of thirty-seven studies involving a total of 3,029 patients found that high doses of outpatient methadone had greater efficacy than lower doses in sustaining heroin abstinence.
- Methadone was also preferable to buprenorphine for this purpose.
- Buprenorphine seems less likely to induce neonatal abstinence syndrome when pregnant women are treated.



Pros and Cons: Methadone and Buprenorphine

- Public and media concern about methadone diversion and potential overdose hazards fuel political pressure to uphold strict and complex regulations on methadone service delivery.
- Methadone clients typically must demonstrate treatment compliance for two years to be eligible to take home a month's supply of medication.
- Buprenorphine has less burdensome regulation and oversight requirements, allowing for home treatment much sooner.



Pros and Cons: Methadone and Buprenorphine

- The side effect profile of buprenorphine appears milder overall than methadone.
- Methadone frequently causes chronic sweats, constipation, and sexual dysfunction.
- A study comparing sexual dysfunction in male patients dependent on heroin with those on methadone or buprenorphine found that fewer patients on buprenorphine reported sexual problems.



Pros and Cons: Methadone and Buprenorphine

- Methadone has been used widely for over thirty years, so much is known about long term effects. Buprenorphine was approved for opioid treatment in 2002, so the long-term effects of maintenance are less certain.
- Buprenorphine is fairly expensive. A month's supply of a typical daily dose of 8-24 mg. sublingually may cost \$200 to \$450 per month.



Pros and Cons: Methadone and Buprenorphine

- Buprenorphine exhibits ceiling effects on respiratory depression due to its intrinsic agonist/antagonist effects. This exceptional pharmacology offers an enhanced safety profile compared with methadone.
- However, buprenorphine-induced respiratory depression may be extremely difficult to reverse when it does occur.
- Buprenorphine has extremely high mu receptor affinity against even naloxone.



Pros and Cons: Methadone and Buprenorphine

- Fatal respiratory depression has been reported among addicts misusing buprenorphine intravenously, often together with benzodiazepines.
- Respiratory depression from buprenorphine may outlast the reversal effects of a naloxone bolus or short infusion, so sustained infusion may be required.



Pros and Cons: Methadone and Buprenorphine

- Buprenorphine exhibits poor gastrointestinal absorption (buprenorphine is administered sublingually in addiction treatment).
- Usually, buprenorphine is used as a combination preparation with naloxone (naloxone exhibits comparatively poor sublingual absorption) in order to prevent illicit injection.
- Thus, buprenorphine poses much less overdose hazard if ingested intentionally or accidentally by non-tolerant individuals.



Pros and Cons: Methadone and Buprenorphine

- Chronic liver disease (especially Hepatitis C) is extremely common in the U.S. among injection drug users.
- Methadone maintenance has proven safe for patients with stable chronic liver disease, including advanced cirrhosis, often with little or no alteration in dose.
- However, sublingual buprenorphine is associated with elevated liver enzymes.



Dual Diagnosis Explained

- Definition: A person who has both an alcohol or drug problem and a psychiatric problem is said to have a dual diagnosis.
- To recover fully, the person needs treatment for both problems.
- According to the Journal of the American Medical Association (JAMA), 37% of alcohol abusers and 53% of drug abusers also have at least one serious mental illness.
- Also, of all people diagnosed as mentally ill, 29 percent abuse either alcohol or drugs.



Psychiatric Problems Commonly Associated with Increased Risk of Substance Use Disorders

- The following table is based on a National Institute of Mental Health study, lists seven major psychiatric disorders and shows how much each one increases an individual's risk for substance abuse.
 - Personality disorder -15.5%
 - Manic episode - 14.5%
 - Schizophrenia -10.1%
 - Panic disorder - 4.3%
 - Major depressive episode - 4.1%
 - Obsessive-compulsive disorder - 3.4%
 - Phobias - 2.4%



Economics Pressures May Exist Toward Injection Drug Use

- Most drugs are very expensive to start with.
- As addiction progresses, tolerance grows, and more drugs needed to achieve the same effect, expense increases greatly over time.
- Drugs administered intravenously are typically about twice as potent as drugs ingested, and also may have a more rapid onset of action.
- A person who starts out eating pain pills or snorting opiates may face mounting economic pressure to begin injecting just to be able to afford enough drugs to avoid withdrawal.



HIV Transmission and Injecting Drug Use

- Needle use can cause HIV to spread explosively through drug using populations. Part of the reason is that IDU's often form very tight-knit groups with close social contacts for drug buying, transport and distribution.
- In the Ukraine, the HIV infection rate among IDU's increased from 0% in 1994 to an estimated 31-57% less than two years later.
- Needles are not the only culprits. Almost any part of the paraphernalia used to prepare drugs for injection may be contaminated.



Hepatitis C Overview

- Hepatitis C Virus (HCV), infects about 170 million people worldwide, about four times as many as HIV. An estimated 4 million in the U.S. are HCV infected at some point in their lives, with 2.8 million active carriers of the virus. Causes 8,000 to 10,000 deaths annually in the United States.
- A screening test for blood became available in 1992, but many people were infected before the blood test was developed.
- Low incidence of liver cancer in the U.S. but the rate is rising due to HCV, THE most common reason for liver transplantation in the U.S.



Cancer of the Liver

- Called Hepatoma or Hepatocellular Carcinoma
- 75% of these tumors are found in association with cirrhosis of the liver.
- Low percentage of cancers in North America, but the rate is rising due to Hepatitis C Virus.
- In parts of Asia and Africa liver cancer comprises 20-30% of all cancers – these are areas of the world where viral hepatitis is common.



Hepatitis B (HBV)

- The HBV infection pattern is much like HIV. HBV is transmitted by blood contact with infected blood, semen, or vaginal fluids.
- In fact, one of the first theories about AIDS was that it was caused by a mutant hepatitis B.
- The risk groups: IDU sharing needles, syringes, spoons or water to inject drugs and straight or gay men or women having unprotected sex
- However, HBV is much more infectious than HIV.



Local Needle Effects

- Abscess
- Cellulitis
- Phlebitis
- Black Tar Heroin “Mexican Mud”
 - More prevalent on West Coast, Southwest
 - Often the reasons people go to HIV testing facilities in San Francisco is the abscesses.
 - Severe abscesses can occur even with sterile injecting equipment.
 - Botulism has been reported.



Bacterial Endocarditis

- Infection of the heart lining, valves
- Often unusual microbes in IVDU: Candida (yeast) Staph endocarditis is also common
- Can also result from dental neglect
- Long term heart valve damage is possible, which may be severe enough to require open heart surgery for valve replacement
- Long courses of IV antibiotics needed



Dental Decay

- The overwhelming majority of dental decay seen in drug clients stems from factors predating drug treatment.
- Dental problems are NOT minor! There is risk of bacterial endocarditis, especially in those with damaged heart valves (previous endocarditis or other reasons).
- Pain due to untreated dental conditions may predispose to relapse.



STD Rates

Title: Prevalence of sexually transmitted infections and associated risk factors among populations of drug abusers.

Authors: Hwang Lu-Yu ; Ross Michael W; Zack Carolyn; Bull Lara; Rickman Kathie; Holleman Marsha.

Publication: Clinical Infectious Diseases. 31(4).
October, 2000. 920-926.

A survey (cross-sectional type) was conducted of sexually transmitted diseases (STDs) and risky behaviors among 407 drug abusers in treatment facilities in 1998.



STD Rates

- Percentages of patients testing positive:
 - HSV-2, antibodies 44.4%;
 - HCV, antibodies 35.1%;
 - HBV, antibodies 29.5%;
 - HIV, antibodies 2.7%.
 - Syphilis antibodies 3.4%;
 - Chlamydia nucleic acid, 3.7%;
 - Gonorrhea, nucleic acid, 1.7%.



STD Rates

- Out of 407 subjects, approximately 62% had markers for one of the STDs.
- Statistical analysis (logistic regression) was used to identify demographic / behavioral associations
- Conclusion: High prevalences of STDs among drug abusers indicate the need for integration of STD screening and treatment into drug treatment programs.



Summation of key points

- The primary care practitioner is often called upon to distinguish between appropriate use and misuse of opioid pain medication.
- Addiction and dependence are not the same thing, and this is a vital distinction.
- Methadone and buprenorphine can both be useful agents depending upon the specific needs and history of the individual patient.
- Opioid use disorders are associated with a wide range of psychiatric and medical diseases that are seen often in primary care.