

# Knowledge Workbook I

## Addiction Medication and Chemical Dependence Treatment: Incorporating Addiction Medication into Addiction Treatment

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OFFICE OF ALCOHOLISM & SUBSTANCE ABUSE SERVICES  
*Addiction Services for Prevention, Treatment, Recovery*

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## Introduction

The chemical dependence treatment system has had limited exposure to the effective use of medications in the treatment of addictions. The general experience has focused on the use of medications to ease withdrawal, as well as antabuse for alcohol dependence and methadone for opiate dependence. Historically, abstinence-based and drug-free treatment meant the elimination of use and/or reliance on medication.

This experience started to change when the addiction treatment system began effectively treating persons with co-occurring disorders. The role of medication in the mental health system was to normalize the patient's cognitive and emotional responses to more fully allow behavioral treatment to be successful. The combination of the psychotropic medications prescribed by mental health professionals and the addiction treatment offered by the addiction professional yielded better results than either treatment alone. This successful integration of medicine and behavioral treatments provides one key to unlocking the future of successful addiction treatment.

Some providers struggle with a confused philosophical approach to addiction treatment and the use of medication. With advancements in the study of neuroscience and addictions, and the development of new addiction medicines, the ability of providers to address the addictive compulsions, including craving, withdrawal and obsessive thoughts is significantly increased. There is clear evidence that addiction medicines should be incorporated into mainstream addiction treatment. To do so will require reliable information learned from the clinical trials and the integration of these medical protocols with behavioral treatment. Most importantly, both treatment providers and patients need to learn that these are medications, not drugs that are being recommended.

Within the addiction field, there is debate about referring to those we treat as clients, consumers or patients. This workbook uses the term patient to emphasize the science of addiction, as well as the medical approaches and consequences of the use of addiction medicine. The term patient is never meant to de-emphasize our commitment to ensuring the integration of addiction medicines into the clinical, behavioral treatment plan.

# Addiction Medicine Workbook

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# CHAPTER ONE

## How Can This Information Help?

Learning about addiction as a "brain disease" is exciting. As they learn more about the neuroscience of addiction, scientists are able to develop addiction medicines. The use of these medicines must be integrated into a treatment plan which includes cognitive, behavioral treatment. Understanding how addiction impacts brain functioning, and using addiction medicines as one component of treatment may necessitate making adjustments in both the treatment program and in the way you work.

### Benefits and Adjustments to Consider as Program Managers

- Ensuring the development and implementation of training curricula about addiction medicine that include the science of addiction, medical signs, symptoms and medical consequences of drug abuse.
- Improving cross-training and the integration of knowledge and interventions between medical staff and counselors.
- Re-designing/modifying program tools (e.g. treatment plans) and processes (e.g. scheduling) that both incorporate addiction medicines and specific patient needs when taking these medications and/or during withdrawal.

### Benefits of Learning About Addiction Medicine for Counselors

- Understanding the changes in the functioning of the human brain of those with addictive disorders.
- Increased understanding of how and why some patients' drug use can mask psychiatric symptoms.
- Increased competence from understanding how neuroscientific changes in the brain contribute to relapse.
- Improved ability to communicate with medical professionals about medications.
- Ability to offer the patient information about emerging drug therapies, as well as, help the patient learn about the changes that have been caused in his/her brain.
- Improving the rates of retention and completion of treatment.
- Improved diagnoses and individualized treatment plans that meet the specific needs of each patient.

## Possible Counselor Adjustments to Consider in Treatment and Treatment Plans for Patients who are Taking Addiction Medicines

- Maintaining an on-going therapeutic alliance between medical staff and counselors where all staff are responsive to patient concerns.
- Briefer/fewer group & individual sessions during early phase of treatment if your patient is adjusting to addiction medication(s) and/or drug(s) of abuse withdrawal because of cognitive impairment as a result of the withdrawal process and/or the medications.
- Closer counselor observation to monitor side effects of the medications and possible medical conditions that might appear as relapse symptoms, (e.g. Are these flu symptoms an interferon side effect or opiate withdrawal?).
- Greater attention and awareness of the patient's physical symptoms and closer relationship with medical staff to change dosage or medications.
- Developing an individualized treatment plan that takes into account the specific type of drugs of abuse and addiction medicines used, given that changes in the brain chemistry may result in markedly different cognitive or behavioral abilities.
- Including medication adherence as part of the treatment plan to ensure compliance.

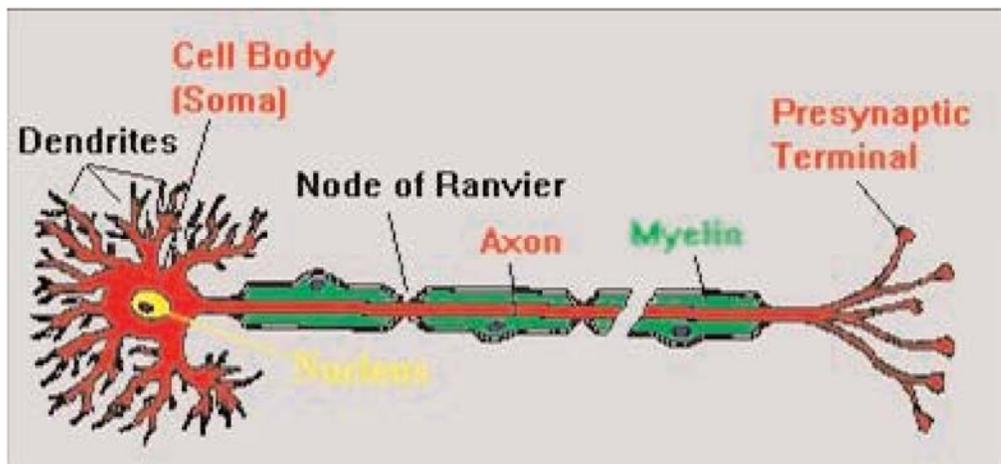
## CHAPTER TWO

### Addiction is a Disease of the Brain

To understand addiction science, you need to know about neurons, neurotransmitters & brain receptors. Brain activity is chemical activity.

#### Neurons

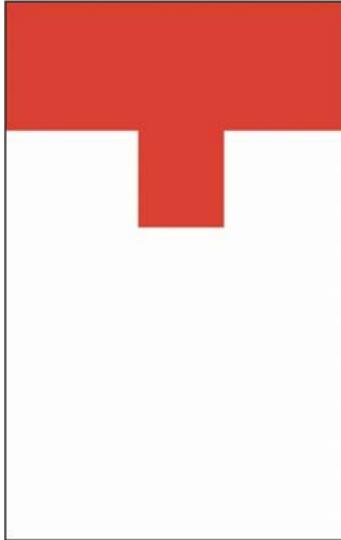
A neuron is the basic unit of the nervous system. It is composed of a cell body, the dendrites or axon terminals (branches that receive impulses from other neurons and axons) and the axon (which makes contact with dendrites from nearby neuron). Reactions are caused by the release of chemicals that exert influence on a neuron. Axons have tiny vesicles (synaptic vesicles) or sacs that contain molecules of a specific transmitter. The contents of the sacs are released into a narrow area (synapse) between the axon of one neuron and the dendrite of the next neuron. The system is like an electrical wire that ends near another wire. But electrical current doesn't jump into the opening. Instead, a transmitter is released and sets in motion activity on the next unit. The signals are based on chemical and electrical shifts across the neuron membrane.



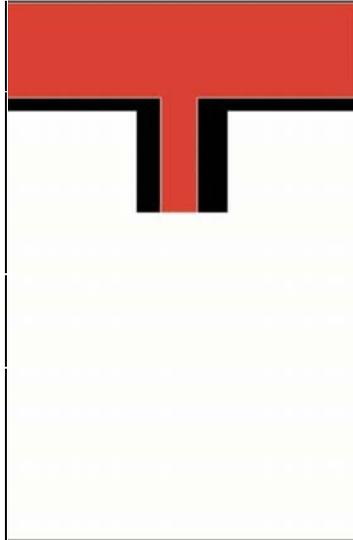
Neurotransmitters & Brain Receptors: Neurotransmitters react at binding sites called brain receptors. When the neurotransmitter binds to the receptor, the site is activated with an excitatory or inhibitory effect.

To understand the neurotransmitter and receptor system, you need to know about:

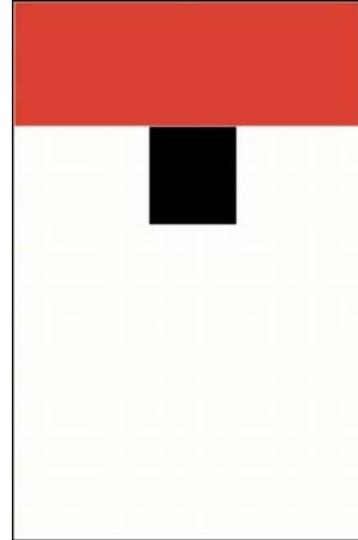
**Full Agonist** - A compound (drug, medication, neurotransmitter) that activates a receptor in the brain. This is like putting a key in a lock and opening the door.



**Partial Agonist** - A compound similar to a full agonist because it binds to the receptor and activates it. At low dose, a full or partial agonist is indistinguishable from each other. But at a higher dose, the partial agonist is less effective than a full agonist. The key unlocks the door, but it does not open.



**Antagonist** - A compound that binds to a receptor and effectively blocks it (prevents activation by an agonist). This is like putting a key in the lock which prevents another key from entering the keyhole, but neither opens the door.



## Important Terms to Know

**Affinity** - Strength with which a drug binds to its receptor. This does not necessarily mean activation.

**Dissociation** - Measure of the disengagement or uncoupling of the drug from the receptor.

**Tolerance** - A decrease in subjective and objective effect of the same drug and same dose when used over time. With tolerance, one has to increase the dose to achieve the same desired effect.

**Physical Dependence** - A characteristic set of withdrawal signs and symptoms upon reduction or cessation of the administered compound.

## Important Neurotransmitter Systems to Know

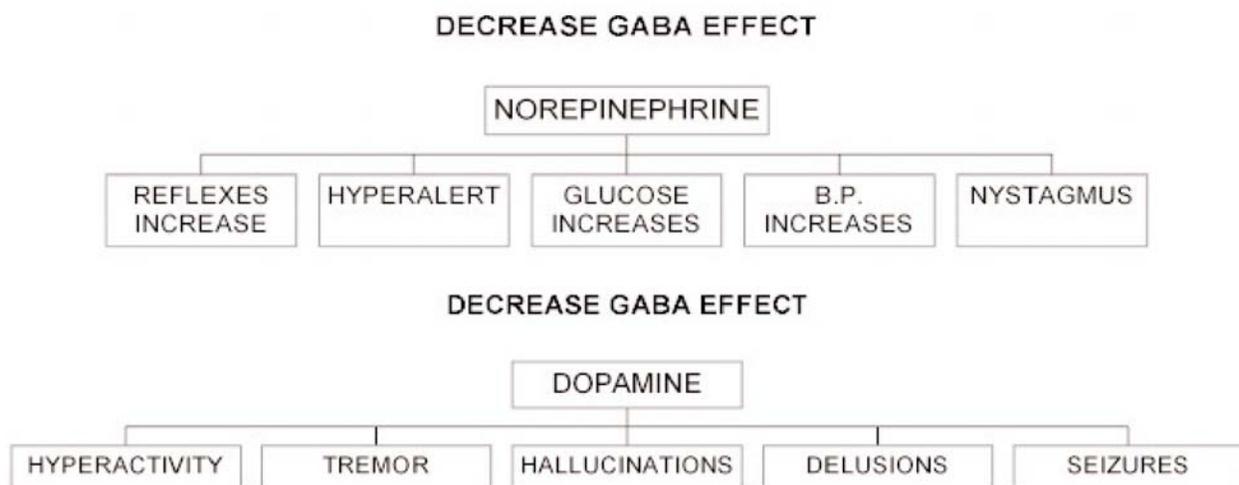
**GABA (Gamma aminobutyric acid)** is often affected by drug use. It is an inhibitory neurotransmitter because it down-regulates or turns down responses and functioning. Barbiturates and benzodiazepines (e.g. valium and librium) work through this transmitter.

**Dopamine and Norepinephrine are stimulatory chemicals**, which turn up responses and functioning. In an unaffected brain, the neurotransmitter systems are typically in relative balance, responsible for gentle mood swings and stabilization.

*Sedatives are down-regulators or depressants.* Use of sedatives mimics the inhibitory effect of GABA. When someone uses a sedative, the brain decreases (inhibits) GABA production. When the sedatives are stopped, there is nothing in the brain to keep responses and functioning low, and the individual experiences agitation, trembling and anxiety until the brain is able to produce more GABA.

## Norepinephrine and Dopamine are controlled by GABA

Norepinephrine (NE) is a stimulatory chemical that regulates mood, maintains the sleep state and causes constriction of blood vessels. Too little can cause depression; too much can cause mania and/or anxiety. Dopamine (DA) can also modulate mood and thought processes. It is involved in the pleasure pathway (mesolimbic system).



## More About Neurotransmitters

*When the sedative abuser withdraws or suffers GABA depletion,* the excess of norepinephrine causes an increase in reflexes, glucose, blood pressure and eye twitching. With too much dopamine, the abuser will develop hyperactivity, tremors, hallucinations, delusions and seizures. This is untreated sedative withdrawal.

*To treat the withdrawal,* patients are given pharmacological equivalents of the abused sedatives to prevent GABA deficiencies; it slows down the development of norepinephrine and dopamine excess, easing withdrawal symptoms.

**Dopamine and Cocaine:** When the neuron that makes and releases dopamine is exposed to cocaine, the neuron is unable to pick up the dopamine that is released for future use (re - uptake inhibition). This causes excess dopamine in the synapse of the neuron (area between two neurons) and more dopamine exposure on the second neuron. Excess dopamine causes greater activity in the pleasure pathway (the high); the loss of dopamine causes depression. This is the cocaine user's cycle.

**Dopamine and Heroin:** Heroin increases the release of dopamine and pleasure increases, providing positive reinforcement.

*Dopamine* levels are increased in patients who suffer from schizophrenia. Those who suffer from Parkinson's disease and depression have lower levels.

## Serotonin Receptor System

Serotonin is found in plants and animals. It is located in the central nervous system, the walls of the intestine and in blood vessels. It complements the excitatory systems of dopamine and norepinephrine.

*Each receptor has different effects when triggered.*

- Serotonin modulates moods, controls appetite, initiates sleep, controls temperature, and effects sexual and hallucinogenic behavior through cardiovascular function and muscle contractions.
- Serotonin 5 - HT1A Receptor System is in the central nervous system and increases male sexual behavior, lowers the blood pressure and increases food intake. It also decreases body temperature and anxiety.
- Serotonin 5 - HT1C Receptor System will affect the heart and cause a decrease in pain sensation and induce sleep.
- Serotonin 5 - HT1D Receptor System is involved with blood vessels. Medications that act like serotonin have been developed to work at this site to treat migraine headaches.

## More About Serotonin

*Why are serotonin and serotonin receptors important to the chemical dependence professional?* A decrease in serotonin or inefficient serotonin receptors may cause depression. If the receptor can be made more efficient or we can cause an increase in the serotonin at the receptor, we can treat depression in our patients. The group of antidepressants (Prozac, Paxil, etc.), which increase available serotonin, work in this manner. Other medications increase the efficiency of serotonin in the other receptor site, such as Buspar.

Many medications are based on "serotonin" chemistry. Below are some examples:

- ***Sumatriptan (Imitrex)*** is used to treat migraines as it triggers the receptor and causes constriction of the blood vessels.
- ***Fenfluramine (Pondimin)***, of Fen-Phen fame, is an appetite suppressant by depleting serotonin.
- ***Clomipramine (Anafranil)*** for Obsessive-Compulsive Disorder inhibits norepinephrine and serotonin reuptake.
- ***Venlafaxine (Effexor)*** inhibits norepinephrine, serotonin and dopamine reuptake to treat depression.
- ***Ecstasy (MDMA)*** may deplete serotonin. It is a neurotoxin.

All hallucinogens work through the serotonin system.

## Opiate Receptors

Emerging addiction medications also work on another important system in the brain, the opiate receptor system. The brain manufactures many opiate-like chemicals naturally. The most common are endorphins, enkephalins and dynorphins. These opiate-like substances work at the opiate receptors in the brain and initiate various opiate-related effects. Of the many opiate receptors, those most understood at this time are:

- ***Mu receptor*** is activated by endorphins, morphine and other opiates. Such activation leads to the individual experiencing euphoria, a decrease in feelings of physical pain, depression of the respiratory system and pinpoint pupils.
- ***Kappa receptor*** is activated by morphine, dynorphins and many of the partial opiate agonist/antagonists (e.g. pentazocine and buprenorphine). An agonist is a chemical that acts like a neurotransmitter. An agonist/antagonist is a chemical that has both some positive effects on the receptor and some negative or blocking effects. Stimulation of the Kappa receptor produces feelings of both pleasure and depression by decreasing dopamine.
- ***Delta receptor*** stimulation causes decreased feelings of physical pain and some pleasure. The enkephalins work at this site.

# CHAPTER THREE

## Drugs of Abuse Primer

Patients abuse many drugs. To understand their effects, it is easiest to learn about classes of drugs, rather than each individual drug. While addiction is a "brain disease," it is also important to know the physical signs and symptoms and medical consequences of drug use and/or abuse.

The nine major drug classes are described in this chapter.

Alcohol, Sedative/Hypnotics, Opiates, Stimulants, Hallucinogens, Cannabinoids, Dissociative Anesthetics, Inhalants/Solvents, Anabolic Steroids

### ALCOHOL

#### Signs & Symptoms/Levels of Blood Alcohol

Alcohol is a depressant that affects all parts of the body. People use alcohol to feel pleasure, decrease anxiety and sexual inhibitions, and often to relax. (In the later stage of alcohol dependence, alcohol may be ingested to decrease uncomfortable withdrawal symptoms.) An intoxicated person will show certain signs and symptoms depending on the level of alcohol in their blood (measured as a percentage of alcohol present in the individual's bloodstream). For example, a person with a blood alcohol level greater than .15, who shows no signs or symptoms of intoxication, is usually alcohol-dependent, as is someone who can actually drink enough to reach levels greater than .30.

#### Signs and Symptoms by Blood Alcohol Concentrations (BAC):

|            |  |
|------------|--|
| .02 - .09: | Loss of muscular coordination  |
| .10 - .19: | Neurological impairment, impaired gait, prolonged reaction time, mental impairment and lack of coordination. |
| .20 - .29: | Nausea, vomiting, worsening gait and impairment  |
| .30 - .39: | Decrease in body temperature, difficulty speaking, amnesia, stupor   |
| .40 >:     | Coma   |

*Alcohol is broken down in the stomach and by the liver at a rate of 1/3 of an ounce per hour.* One beer will raise the blood alcohol level .015. Therefore, 3 beers consumed in one hour will result in a blood alcohol level of about .045. The alcohol level drops by .015 per hour.

## Signs and Symptom of Withdrawal

- Alcohol withdrawal can start at 6-60 hours after the last drink.
- Signs and symptoms of withdrawal include tremors, nausea, decreased appetite, anxiety, weakness, insomnia, inattention, flushed face, redness of eyes and increase in reflexes.
- The treatment of withdrawal requires support and the occasional use of medication. The patient must always be evaluated for other illnesses or injuries. Treatment of withdrawal only helps the body to repair itself, but for recovery, the patient must enter into continuing treatment.
- Withdrawal may be complicated by illusions, hallucinations and seizures. Illusions are misinterpretations of the surroundings and effect up to 25% of withdrawal patients. For example, the patient may think he/she sees wavy lines at the corners of walls. Hallucinations are less common and are described as tactile (feeling something), olfactory (smelling something) or visual (seeing something). In all cases, the perception is not real. The patient has a clear mental status and is upset by the illusion or hallucination.
- Seizures, or "rum fits," as they were called in the past, are usually singular; only 25% are multiple. The patient may complain of heightened light sensitivity during the period when he/she is most vulnerable to a seizure occurrence. Thirty percent (30%) of patients that have withdrawal seizures go onto delirium tremens (DTs).
- Complicated withdrawal can be accompanied by delirium tremens if there is motor hyperactivity (tremors, restlessness, agitation and increased reflexes), autonomic hyperactivity (increased heart rate and blood pressure, profuse sweating and dilated pupils), profound confusion, disorientation, hallucinations and paranoid delusions. The risk of delirium tremens is increased if the patient has a blood alcohol level greater than .30 or withdrawal seizures. The mortality of untreated DT's is 10 -15%. If treated, the mortality is 1 - 2%. DT's should always be treated as an emergency and in an intensive care-like setting.
- Persistent mild withdrawal is characterized by a patient complaining of sleep disturbances, a mild tremor, anxiety and depression. This can last for weeks or months after the last drink. It will get better if the person stays sober.

## What is a Hangover?

Alcohol Hangover, or Veisalgia, is derived from the Norwegian word "Kveis" for uneasiness following debauchery and the Greek word "algia," meaning pain. The hangover has been known since biblical times, "woe unto them that rise up early in the morning, that they may follow strong drink" (Isaiah 5:11).

Possible medical causes of hangover include: dehydration, inflammation caused by the release of cytokines from white blood cells, build up of acetaldehyde, decreased glucose and the hyper-excitable state of the brain the day after drinking. This state happens because alcohol suppresses brain activity and then there is a rebound - hyperactivity.

The symptoms of a hangover include:

- headaches (66%)
- poor sense of well-being (60%)
- poor appetite (21%), tremors (20%)
- fatigue (20%) and nausea (9%)
- increased heart rate
- impairment of thinking and visual-spatial relationships
- lightheadedness and dizziness upon arising

Hangovers have a significant economic impact. There is an increased risk for injury and poor job performance from decreased visual-spatial skills, decreased dexterity, decreased management skills and decreased task completion. It has been reported that 29% of all college students have lost school time awaiting hangover recovery.

### Medical Consequences of Alcohol Abuse

- ***Nervous system:*** Too much alcohol can cause insomnia, night terrors and frequent awakening. Long-term alcohol abuse can lead to chronic organic brain syndrome (fatigue, anxiety, depression, memory loss and confusion), cerebellar degeneration (loss of tissue in the part of the brain that controls fine movements); optic neuropathy (damage to the optic nerve that can cause loss of vision, blurred vision and loss of color vision); strokes from increased blood pressure and increased blood clotting and blackouts (short-term memory loss).
- ***Lungs:*** Because it suppresses the cough reflex, stomach contents can be aspirated into the lungs. White blood cells function poorly; pneumonia and TB can occur. The use of cigarettes can compound respiratory problems.
- ***Heart:*** Since long-term alcohol abuse can cause arrhythmia (irregular heartbeat), it can lead to more serious heart problems. Longer-term consumption may result in alcohol cardiomyopathy or heart failure. Cocaine and alcohol used together can increase blood pressure.
- ***Liver:*** One-fifth of alcoholics develop significant liver disease, most commonly seen as a "fatty liver." Liver enzymes must be measured to determine diagnosis. Alcohol hepatitis is a more serious inflammation of the liver and causes nausea, vomiting, anorexia, abdominal pain on the upper right side and intermittent fever and jaundice and can lead to cirrhosis (scarring and fibrosis of the liver). Symptoms include all those previously noted, as well as gynecomastia (enlarged breasts), testicular atrophy, ascites (fluid on abdomen), poor clotting, esophageal varices (dilated veins in the esophagus), confusion and coma.
- ***Stomach:*** Alcohol can affect the esophagus by increasing acid production in the stomach and causing heartburn and reflux. If very severe, the esophagus can rupture and contents of the

stomach may go into the chest cavity. Alcohol can cause erosive gastritis and ulcers. Forty percent of all pancreatitis (inflammation of the pancreas) is caused by alcohol. It can cause abdominal pain, nausea, vomiting and diarrhea. Lack of pancreatic enzymes leads to non-absorbed fat and sugar in the small intestines which causes diarrhea and malnutrition.

- ***Skeleton:*** Alcohol can decrease potassium and phosphate levels, inhibit the use of carbohydrates by the muscle and cause alcohol myopathy (discomfort in the extremities, muscular pain, muscle tenderness, muscle edema and swelling). Alcohol can also affect the calcium metabolism in the bones, causing osteoporosis.
- ***Skin:*** Consequences of alcohol use include premature aging, severe itching, palmar erythema (red palms) and spider angiomas (dilated blood vessels on the chest).
- ***Other medical effects include:*** breast enlargement in men at the end-stage of liver disease, testicle atrophy (small testicles), peripheral neuropathy (numbness and tingling in hands and feet), depressed bone marrow and impotence.

## SEDATIVE/HYPNOTICS

Sedative/hypnotics are used to decrease anxiety, induce sleep and offset effects from other drugs. Benzodiazepines are the most commonly abused sedative/hypnotics. Sedative/hypnotic intoxication is usually manifested by a decrease in anxiety, sedation, with occasional elation secondary to depression of inhibitions, and judgment. Pupils are neither dilated nor constricted and are slowly reactive. Hiccups are seen in long-term benzodiazepine use.

Note: There is a sedative, glutethimide, which causes enlarged pupils.

### Signs and Symptoms of Withdrawal

- May occur if a patient uses benzodiazepines or barbiturates (another sedative group) for 4 to 6 months at a therapeutic level or for 2 to 3 months at 2 - 3 times the therapeutic level prior to stopping the sedative.
- Withdrawal from benzodiazepines can last 3 - 5 weeks with signs and symptoms like acute alcohol withdrawal. The timeframes and severity of the withdrawal depends on the dose and duration of drug use. Withdrawal is more prolonged in the older user.
- Withdrawal will be more severe if the drug used is rapidly metabolized or highly potent, like Ativan® or Xanax®. Abrupt discontinuation or decrease can cause severe withdrawal.
- Benzodiazepine withdrawal is further characterized by mood changes, dysphoria, sleep changes such as insomnia and disruptive sleep-wake cycle, increase in pulse rate and in blood pressure, increased reflexes, tremors, restlessness, nausea, ataxia, seizures, postural hypertension, dilated pupils, exaggerated blink reflex (especially from barbiturates), metallic taste, perceptual changes

like illusions, hallucinations, depersonalization, and sensory hyperactivity (bright lights, loud noise).

- When a user of benzodiazepines overdoses, consciousness decreases. There is also a decrease in the breathing rate and the blood pressure. Body temperature may decrease and stomach action may become paralyzed.
- Sedative/hypnotics can have a protracted withdrawal over months. Patients may experience depression, anxiety and panic attacks, ringing in the ears, headaches and dizziness.

### More About Sedative/Hypnotics

- GHB or gamma hydroxybutyrate is best known as a "date rape" drug. It is a clear liquid, white powder, or tablet initially sold to body builders to release growth hormone. It is fast acting; it takes 20 minutes for the sedative effect and lasts 4 hours.
- Rohypnol is also one of the first "date rape" drugs. It is in the benzodiazepine class and dissolves easily in carbonated drinks, causing significant amnesia for up to 12 hours.
- GBL or gamma butyrolactone is marketed as an industrial solvent used to clean circuit boards and degrease engines. It is metabolized into GHB by the body.

## OPIATES

Opiates are most commonly used to treat severe or chronic pain. Opioid abusers experience feelings of sedation, euphoria, analgesia, or "the rush." When intoxicated with opiates, someone may experience a decrease in blood pressure, breathing rate and heart rate, as well as euphoria and pinpoint pupils. Initially, they may look like they are dozing or "nodding off."

Signs and Symptoms of Opiate Withdrawal are described in three phases:

1. Early: yawning, sweating, teary eyes and runny nose.
2. Middle: restless sleep, dilated pupils, gooseflesh, tremor, irritability and lack of appetite.
3. Late: an increase in early and middle signs and symptoms; an increase in heart rate and blood pressure, nausea, vomiting, diarrhea, abdominal cramps, labile mood, depression, muscle spasm, weakness and bone pain. However, even in the late phase, opiate withdrawal, which is a serious medical condition, is rarely life- threatening.

*Note: These signs and symptoms are time-related, rather than related to the severity of the withdrawal as specified in the OASAS 816 regulations for Crisis Services.*

### More About Opiates

- Heroin (one of the most commonly used opiates) withdrawal usually starts 8 - 12 hours after the last use and peaks in 48 hours. The actual withdrawal period can last from 5 to 10 days. In

methadone (another opiate) users, there is a protracted withdrawal that can last for up to 9 months. It is characterized by weight gain, and increases in the breathing rate, blood pressure and basal metabolic rate. There is a decrease in body temperature and frequently menstrual irregularities.

- Opiate detoxification regimens rely on many medications to treat associated complaints. Another effective method of treatment is pharmacologically based, using methadone, with a stabilization period followed by a slow reduction in the medication.
- Meperidine, or Demerol®, is an opiate pain medication that was used in post-operative patients until it was found that it had a metabolite, normeperidine, which is especially toxic if used in combination with MAO inhibitors. This combination of medications can cause seizures, tremors and confusion.
- Illegal labs that were making meperidine analogs incorrectly synthesized one into a chemical called MPTP; its use leads to an irreversible Parkinson's Disease-like state.

### Opiate abuse has medical consequences

- Effects from drug injection can include infections, blood clots and chronic swelling.
- Infected dirty needles can cause hepatitis B & C and AIDS.
- Other consequences may be skin tracks, scars, lesions, skin swelling, skin death, constricted fingers, infected veins, infected joints and endocarditis.

## STIMULANTS

Users of stimulants, like cocaine and amphetamines, are frequently looking for euphoria, increased alertness, a feeling of well being, increased energy, a decrease in weight, decreased appetite and heightened sexuality.

### Sign and Symptoms of Stimulant Intoxication

- dilated pupils
- increased heart rate (30-50%)
- increased blood pressure (15-20%)
- nausea and vomiting
- confusion
- tremors
- weight loss
- chest pain and irregular heart rates
- abnormal EKG's
- headache (most common neurological complaint)

- seizures (can occur at the first use of cocaine, but seldom after a one-time use of amphetamines)
- priapism (penile erection that is sustained with possible tissue damage)
- kidney failure
- in the chronic amphetamine abuser, the patient has constipation, inability to urinate, jerky movements during sleep, jaw clenching and teeth grinding, nausea and vomiting, headaches, increase in pulse rate with decrease in blood pressure, psychosis (which can last for months) and cerebral hemorrhage

*An overdose of stimulants can be life-threatening.* All the signs and symptoms previously noted may be experienced more severely and are, therefore, more dangerous. Overdose can lead to heart attacks and stroke. There may be a dangerous increase in the body temperature, which usually means a worse prognosis.

### Signs and Symptoms of Stimulant Withdrawal

Withdrawal in the stimulant user is usually not severe and not life-threatening. The person going through withdrawal may complain of fatigue, unpleasant dreams, insomnia or a need to sleep all day, increased appetite and anxiety. There is no proven medical regimen for the treatment of withdrawal in this class of drugs.

### More About Stimulants

- *Nicotine*, a colorless to pale yellow compound with a pungent odor, is a stimulant. It is absorbed through the skin and respiratory tract. Nicotine is bound to its vehicle, either the tobacco leaf or in the case of nicotine gum, polacrilex. A cigarette has 10 mg of nicotine; approximately 1 mg is delivered to the smoker per cigarette.
- *Nicotine is an addictive substance.* On a milligram per milligram basis, it is ten times more potent than heroin due to its positive reinforcing effect.
- *Nicotine intoxication* has as its possible features: nausea, vomiting, abdominal pain, diarrhea, sweats, flush, dizziness, confusion, weakness and palpitations.
- *Nicotine withdrawal* is seen as an anxiety state in 87%, irritability in 80% of users and also restlessness, difficulty concentrating and cravings. Withdrawal occurs when the nicotine level has dropped below the critical blood level for the brain (early morning withdrawal in smokers).
- *Medical consequences to nicotine are predominately due to acute stimulant effects.* The significant medical consequences are due primarily to the tar, chemical additives and other by-products of smoking cigarettes and cigars, rather than due to the nicotine itself.
- MDMA or Ecstasy is a frequently abused amphetamine. It is methylenedioxymethamphetamine and was developed as an appetite depressant. It appears to damage serotonin - transmission

sites. Users report nausea, jaw clenching, teeth grinding, tremors, blurred vision, tics, increased heart rate, anxiety, altered time perception, increase in social interactions and decrease in the amount of sleep that is needed. The user may become very paranoid. A hangover the day after use may include insomnia, drowsiness, fatigue, sore jaw muscles, headaches and loss of balance.

- Khat or methcathinone is a drug that appears to have a combination of drug class effects. The user experiences higher blood pressure, temperature and heart rates. There may also be tremors, twitches and a flush. There is an urge to urinate, dry mouth and increased sexual desire. There is often a decrease in appetite and massive weight loss. Psychologically, the user can complain of anxiety, confusion, extreme paranoia, hallucinations and grandiosity. Seizures have been associated with the use of this drug.

### Medical Consequences of Cocaine Use

- *Nervous system:* Even a first-time user can experience seizures, a severe headache and bleeding in the brain and stroke.
- *Heart:* Cocaine use can cause atrial irregular rhythm, angina, hypertension, aortic rupture and ventricular rupture.
- *Lungs:* "Crack Lung" often mimics pneumonia with chest pain, shortness of breath, and increased temperature, although the chest x-ray is normal. Pulmonary edema, pneumomediastinum (lung rupture and air leaks), and hemoptysis (coughing up blood).
- *GI system:* Cocaine users often experience stomach pain, nausea and colitis.
- *Other effects:* Cocaine can cause a lack of oxygen to an extremity caused by spasms of the artery that supplies blood to that area. It can also cause depression, anxiety, psychosis and death.

### HALLUCINOGENS

- LSD, Mescaline and Psilocybin are the prototype hallucinogens. LSD is available in the old version, LSD 25, and a new version, "illusion," which causes an increase in visual effects. Mescaline is found in the peyote cactus (*Lophophoria williamsii*, *Anhalonia lewinii* and others). Psilocybin comes from mushrooms. Hallucinogens appear to work through the serotonin system.
- The subjective experience of hallucinogen intoxication is heavily determined by the set (expectations and personality) and setting (environment) of the user. Effects include modifications in perception, hallucinations, distortions ("trails"), greater insight and synesthesia (cross-over or mixing of the senses, "smell a sound"). Onset of hallucinogen effects is usually within one hour, with a peak in 2 - 4 hours.
- Common problems noted from hallucinogen use include: a tolerance that develops rapidly (e.g. 3 - 4 days for LSD), depersonalization, confusion, acute anxiety and panic, depression, flashbacks,

temporary psychosis, loss of coordination, increased pulse rate and temperature, dilated pupils, nausea and vomiting (30 - 120 minutes after mescaline use).

- Flashbacks may be seen with LSD, Psilocybin, Mescaline, PCP and MDMA use. Different studies report from fifteen to seventy-seven percent of users experience brief flashbacks that taper off over time.
- Psychosis seen with hallucinogen use is a paranoid schizophrenia-like syndrome (with visual hallucinations, not auditory as in real schizophrenia). In post-LSD psychosis, one can see schizo-affective disorders.
- There is no treatment for intoxication; there is no withdrawal.

## More About Hallucinogens

DMT is a drug known as the "businessman's LSD." It is a very quick-acting hallucinogen with a total duration of one hour. It is snorted, smoked or used intravenously because it has little effect when taken orally.

## CANNABINOIDS

Cannabis (marijuana) often gives the user a sense of well being or euphoria. Other desired effects include altered perceptions, altered time sense, decrease in sexual inhibition and a modification of the level of consciousness. Research has shown that the cannabinoids appear to work in the brain at the level of the hippocampus. Its use is highly correlated with alcohol use in the adolescent.

Once thought to be a "safe drug," problems with cannabinoid use include: decreased vigilance, decreased motor coordination, decreased strength, increased pulse rate (not blood pressure or temperature) and galactorrhea (breast milk production) in 20% of female users, decreased testosterone, decrease in sperm count and motility, decreased helper t cells, interference with the body's mechanism of fighting off foreign materials like viruses and bacteria, inability to learn, acute panic, delirium, depersonalization, paranoia, hallucinations and flashbacks.

## Signs and Symptoms of Cannabinoid Withdrawal

Cannabinoid use can lead to withdrawal. While not as severe as other drug classes, the user will experience tremors of the tongue and extremities, insomnia and sweats. This usually occurs about 10 hours after last use.

## Medical Consequences

- *Lungs:* Because it is inhaled, its use can lead to all the cigarette-related diseases such as bronchitis and emphysema.
- *Heart:* With initial use, heart rate and blood pressure increase.
- *Reproductive system:* Testosterone may decrease in men; women may have shorter menstrual cycles and galactorrhea (milk in breast tissue).

## PHENCYCLIDINE (PCP)

- Phencyclidine or PCP is a dissociative anesthetic. It has stimulant properties, but many other drug class symptoms are seen with its use. PCP users can experience illusions, hallucinations, feelings of strength and special insights. Unfortunately, many problems occur with use including anxiety, feelings of doom, outbursts of hostility, violence, lack of coordination and paranoia.
- Violence is the #1 cause of death in PCP users.
- PCP intoxication can be described as low, moderate and high dose intoxication. Low dose is characterized as dreamy, mood elevation, panic and impaired judgment. Moderate dose appears as inebriated, dissociated, ataxia, confused, decreased pain and amnesia. High dose includes all of the low and moderate signs and symptoms, as well as hallucinations, catatonia, blank stare, drooling, delirium, psychotic behavior and hypertensive crisis.
- The treatment of PCP is difficult. Disruption of sensory input by PCP causes unpredictable, exaggerated, distorted and violent reactions to environmental stimuli. The cornerstone of treatment is to minimize sensory input for the PCP-intoxicated patient by treating in a quiet and calm environment. Precautionary physical restraints are recommended by some; care must be taken to avoid very high body temperatures and muscle breakdown.
- PCP withdrawal is similar to cocaine withdrawal with depression, drug craving, an increased appetite and increased sleep.
- Ketamine or "Special K" is a shorter - acting drug than PCP, though still in the anesthetic class. It may be used orally or intravenously, but is not smoked like PCP.

## INHALANTS/SOLVENTS

Inhalants and solvents are grouped together because they are considered a "cheap high" and both cause euphoria, excitement and altered perceptions.

Frequently used by a younger group, indications of use include chemical odor on body or breath, paint stains on skin and clothes, hidden containers (whiteout, glue), drunkenness, dizziness, gait impairment, slurred speech, and red runny nose and eyes.

There appears to be no withdrawal with this class of drugs.

## Medical Consequences

- slurred speech
- ataxia, impaired judgment / lack of coordination / kidney and liver failure / primary liver cancer / wheezing
- pulmonary hypertension / heart failure
- sudden death
- irregular heart rate
- cardiac muscle damage (cardiomyopathy)
- atrophy or death of brain tissue
- kidney damage with renal failure
- hepatitis, damage to the bone marrow (where the red and white blood cells are manufactured)
- chemical pneumonia

Some complications include nitrite poisoning where the user complains of severe vomiting, cyanosis (blue tinged skin and lips) and, finally, shock (or unconsciousness).

## Medical Effects by Specific Drug

- Amyl nitrate: anemia (methemoglobinemia)
- Volatile hydrocarbon inhalers: weight loss and pigmented hands and face
- Dimethyl benzene (toluene): Ototoxicity (deafness)
- Hexane (glue), ketones: Peripheral nerve damage
- Nitrous oxide: Multiple sclerosis - like syndrome
- Trichloroethylene: Slowly reversible facial nerve damage.

## ANABOLIC STEROIDS

Anabolic steroids are abused by athletes and body builders. This class of medication is approved for treatment of metastatic breast cancer, to stimulate bone marrow in severe anemia, and to stimulate sexual development for testicular dysfunction.

Body builders and athletes use steroids in several different ways or cycles. "Pyramiding" is when a user builds up to a top dose and then tapers down. "Stacking" is when intravenous and oral preparations are combined (up to 8 different drugs at one time) to limit liver toxicity.

Steroid users frequently use adjuvant medications to limit their steroid side effects. One medication, HCG, limits the decrease in testicle size. Diuretics are used to decrease water retention, frequently a problem with anabolic steroid use.

Anabolic steroids may cause withdrawal with craving, fatigue, depression, restlessness, insomnia, decreased libido and headaches.

### Medical Consequences

- Effects on men and women include hair loss, mood swings, acne, difficulty urinating, hands and feet swelling, weight gain, adenomas in the liver, peliosis hepatitis (blood filled cysts in the liver).
- Effects on men include testicular atrophy, decreased sperm count, infertility, baldness, increased breast size, increase risk of prostate cancer.
- Effects on women include facial hair, changes in menstrual cycle, increased size of clitoris, male-pattern baldness and deeper voice. The side effects in women are usually irreversible.

# CHAPTER FOUR

## Urinalysis Drug Screening

Drug abuse is a chronic disorder; relapse may occur. Patients may deny or minimize drug use. Urine drug testing can determine drug use and is an integral part of ongoing evaluation and treatment, much like glucose levels are important for the ongoing evaluation and treatment of diabetes.

### How long does the drug stay in the body and can be determined from urine drug screening?

|                              |               |
|------------------------------|---------------|
| Amphetamine/Methamphetamine  | 2 - 4 days    |
| Barbiturates (short-acting)  | 2 - 4 days    |
| Barbiturates (long-acting)   | Up to 30 days |
| Benzodiazepines              | Up to 30 days |
| Cocaine                      | 1 - 3 days    |
| Heroin/Morphine              | 1 - 3 days    |
| Marijuana (Chronic Use)      | Up to 30 days |
| Marijuana (Occasional Use)   | 1 - 3 days    |
| Methadone                    | 2 - 4 Days    |
| Phencycline (Chronic Use)    | Up to 30 days |
| Phencycline (Occasional Use) | 2 - 7 days    |

# CHAPTER FIVE

## Diagnostic Lab Tests

Diagnostic Lab tests assist in diagnosing possible medical problems due to drug abuse.

### Chemistry (SMAC)

- Glucose: sugar level for diabetes; patient should be fasting
- Bun/Creatinine: kidney function
- Sodium/Potassium/Chloride/Carbon dioxide: electrolytes for heart, muscle and nerve function
- Liver Function Profile
  - SGOT (AST): If elevated, indicates liver inflammation
  - SGPT (ALT): If elevated, indicates liver inflammation
  - LDH: If elevated, comes from red blood cell, liver or muscle damage
  - Albumin: A decrease shows liver damage or malnutrition
  - Total Bilirubin: An increase shows abnormal liver function or red blood cell damage
  - Uric Acid: If elevated, may indicate gout
  - Amylase/Lipase: Enzymes (proteins) that come from the pancreas. If elevated, the pancreas is inflamed

### Lipids (Cholesterol/Triglycerides)

- Elevation can impact on heart and blood vessels; patient must be fasting.

### Hepatitis Studies

- Hepatitis B Surface Antibody: If positive, shows prior infection with Hepatitis B virus or past immunization.
- Hepatitis B Surface Antigen: If positive, shows current infection with Hepatitis B virus; is a carrier of disease.
- Hepatitis C Antibody: If positive, shows prior contact with the Hepatitis C virus; does not indicate current infection. (A viral load is needed for this determination.)

### CBC (Complete Blood Count)

- **WBC (White Blood Count)**: Elevated in infections and stress-like withdrawal; low if viral illness or immune deficiency.

- **RBC (Red Blood Count), Hemoglobin, Hematocrit:** Measures amount of red blood cells; if low, indicates anemia.
- **Platelet Count:** If low, can contribute to serious bleeding.
- **Indices:** Tells size of red blood cells; helps determine if there is an iron, B 12 or folic acid deficiency causing anemia.

## Syphilis Screen (VDRL)

- If positive, can indicate prior or current infection.

## Hgb A1 C

- Assesses level of glucose in blood over time.
- Blood Levels of Medications
- Assesses concentration of medication in blood; helps rule out possible toxic levels.

## Urinalysis

- Looks for protein, sugar, red blood cells, white blood cells and bacteria; abnormalities may indicate kidney disease or infections.

## PPD (Purified Protein Derivative)

- Injection under the skin to see if a person has come into contact with the tuberculosis bacteria; positive does not mean active TB.

# CHAPTER SIX

## Addiction Medicines

This Chapter includes is a review of addiction medicines that are currently being used or tested for their effectiveness. All of these medications are seen as aids and tools for clinical treatment and to be prescribed to patients/clients as part of a treatment plan that integrates the use of medications with good clinical behavioral treatment.

### Naltrexone

For alcohol abusers: Naltrexone, marketed since 1994 as ReVia, is the first medication since antabuse that has been approved for the treatment of alcoholism. Naltrexone blocks the pleasurable effects of alcohol and reduces craving for alcohol. In one study, subjects used the medication for 10 weeks and abstinence increased from 37% in the control group to 89%. It was also found that if the subjects did drink, the number of drinks dropped from 9.5 to 2.5.

Naltrexone is safe (the most common side effect is nausea), but liver damage can occur if the medication is used in high doses. As the pharmaceutical company stresses in their inserts and in the PDR, counseling or support groups must accompany the use of naltrexone.

For opiate abusers: Naltrexone is also used in opiate-dependent patients. Naltrexone is an opiate receptor blocker or antagonist. Studies have shown that the use of naltrexone in opiate-dependent patients who have significant social and medical consequences, such as physicians, have been the most successful group to use naltrexone. As an opiate blocker, it has a long-lasting effect after oral dosing (1 - 3 days). New research is being conducted by implanting the medication under the skin where the slow release over a 6 - 8 week period increases compliance and success.

### Nalmefene

This medication is currently used in anesthesia to reverse the effects of narcotic pain relievers. A recent study shows that nalmefene, an opioid antagonist, is effective in reducing cravings and preventing relapse to heavy drinking in alcohol-dependent patients. Studies found that patients who received nalmefene were 2.4 times less likely to relapse to heavy drinking than those who received a placebo. Nalmefene is a "universal" opioid antagonist that works on all opioid receptors. It appears to last longer and be more potent in blocking dopamine than naltrexone.

## Acamprosate

Acamprosate, calcium acetyl homotaurinate, is available in Europe and will be marketed in the United States as Campral when approved for this use by the FDA. It works through the GABA system and like naltrexone, it enhances abstinence and reduces "drinking days" in the alcohol-dependent patient. Of great importance is that it is not metabolized in the liver. This will reduce many of the worries of naltrexone for the advanced alcohol-dependent patient with liver disease

## Buprenorphine

Buprenorphine will be approved by the FDA for use in the United States as an opiate detoxification and opiate maintenance agent. There will be two forms of the medication:

- Sublingual (under the tongue) tablet called Subutex®
- Buprenorphine combined with Naloxone called Suboxone®

Buprenorphine combined with naloxone is called Suboxone® and prevents intravenous use of the tablet after crushing. The user would get an antagonist effect of the naloxone, or at the least, a diminished opiate effect.

Pharmacologically, buprenorphine is related to morphine but is a partial agonist (agonist and antagonist properties). The benefit of this is that, like most partial agonists, it has a safety profile that is better than that of the full agonist, such as morphine or heroin. Buprenorphine is much less likely to cause respiratory depression which is the limiting factor in the use of opiates and causes much of the adverse consequences of use and overdose.

Studies are underway to look at the possibility of buprenorphine use to reduce opiate and cocaine craving.

## Clonidine

Clonidine is an agonist. Originally used solely for treatment of hypertension, Clonidine decreases norepinephrine release, thus reducing the heart rate and relaxes and dilates blood vessels, resulting in a lowered blood pressure. Studies have found that clonidine is useful in treating opiate withdrawal, alcohol withdrawal and nicotine dependence, though it is said to be ineffective in benzodiazepine detoxification. Its major side effects are a decrease in blood pressure, dry mouth and sedation. When used for opiate detoxification, symptoms such as lethargy, restlessness, insomnia and craving are not well relieved. A study by Glassman et al, showed that clonidine reduced the intensity of craving for tobacco. Overall, it tends to ameliorate signs and symptoms of withdrawal, although it does not alter the time course of withdrawal. Regimens for detoxification have been tested with both tablets and longer-acting patches.

## Lofexidine

Lofexidine is a medication that is similar to clonidine (used in opiate withdrawal and by some in alcohol withdrawal and nicotine withdrawal treatment protocols). It works through the norepinephrine system and decreases the effect of norepinephrine (used for blood pressure control in the medical patient). While clonidine has major side effects which include sedation and a lowering of the blood pressure which can sometimes prevent it from being used, lofexidine does not have the same impact on blood pressure, and may be a medication with which patients are more compliant.

## Antabuse

Antabuse has the chemical name: Bis (Diethylthiocarbamoyl Disulfide). Antabuse produces a sensitivity to alcohol which results in a highly unpleasant reaction when the individual under treatment ingests alcohol. The mechanism of action is the blockade of the metabolism of alcohol (oxidation). A product of this oxidation is acetaldehyde. If antabuse is taken, the metabolism stops at the point of acetaldehyde production and there will be an increase in the concentration of acetaldehyde 5 - 10 times higher than in normal alcohol metabolism.

The accumulation of acetaldehyde produces the "antabuse reaction." This reaction can range from a flush and throbbing in the head and neck to nausea, vomiting, breathing difficulty, chest pain, heart failure and possible death.

This medication cannot be given to anyone with a history of severe heart disease, psychosis, allergy to antabuse, pregnancy, paraldehyde use or metronidazole use. It must be used with caution in the patient with a history of diabetes, seizures and liver disease. Antabuse can be of benefit when used in conjunction with a comprehensive treatment program for alcohol dependence.

## Gabapentin

Gabapentin is an anticonvulsant sold under the name Neurontin®. It is being used for pain management and anxiety, though some of the more interesting work is in the field of insomnia, a problem that is very common among alcohol - dependent patients. Dr. Kirk Brown is studying its use in alcohol-dependent patients and has had good results in ameliorating the insomnia when increasing this medication, as needed and up to 1500 mg per day.

## Ondansetron

Ondansetron is a medication used to treat nausea in chemotherapy patients and is sold under the name Zofran®. This medication appears to work through the serotonergic system. Serotonin is implicated in alcohol-abuse behavior, especially in regard to the serotonin<sub>3</sub> receptor and its effect on dopamine. If this

receptor could be blocked, there would be a decrease in alcohol-induced dopamine release, resulting in a decrease in alcoholic drinking behavior.

In his work with this serotonin antagonist, Dr. Bankole Johnson found that early onset alcoholics (early age, broad range of antisocial behaviors, and a high family prevalence) did well with ondansetron and naltrexone combined, though this was only studied in 20 patients.

## Methadone

Methadone is a synthetic narcotic that was developed in Germany during WWII. In 1963, Drs. Dole and Nyswander treated opiate addicts with methadone to control craving. In 1972, it was approved by the FDA for the treatment of narcotic dependence. It is a highly regulated medication that can only be prescribed by a licensed clinic or, on an emergency basis, in a general hospital for addiction treatment. It can be ordered by a licensed physician for the treatment of pain as an outpatient. With a very favorable side effect profile, it is an extremely effective and safe medication. Of extra benefit, there is blood - level testing that can help to individualize treatment.

## Zyban® (bupropion hydrochloride, Wellbutrin SR®)

This is the first non-nicotine medication approved for smoking cessation. The medication works on cravings and withdrawal at the brain level through dopaminergic and noradrenergic pathways. It is successfully used alone or in combination with nicotine-replacement medications (patches, gum). The most common side effect is dry mouth and insomnia. It cannot be used in patients with seizure disorders, bulimia, anorexia, pregnancy, allergy to bupropion or those already treated with Wellbutrin®.

# References

For more information on the subjects presented in this workbook, you can go to the following:

- Principles of Addiction Medicine (2nd edition); American Society of Addiction Medicine
- OASAS Addiction Medicine website: <http://www.oasas.state.ny.us/AdMed/>
- National Institute on Alcohol Abuse and Alcoholism: <http://www.niaaa.nih.gov/>
- National Institute on Drug Abuse: <http://www.nida.nih.gov/>