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## OPIOID SAFETY COURSE

(WELCOME)

*(Picture: Welcome)*



**BY STARTING THIS ONLINE OPIOID SAFETY COURSE YOU AGREE TO THE  
TERMS OF THE FULL DISCLAIMER LOCATED AT END OF THE COURSE**

Welcome to the online Opioid Safety Course, part of the Online Chronic Pain Education and Prevention Program. Opioid therapy when used safely can be a very important part of a patient's treatment plan for chronic non-terminal pain. That being said, opioid medications and medications similar to opioids in the wrong hands and when misused can have deadly consequences. Knowledge is power and this course was designed to educate not only patients,

but the community and referring physicians alike on the facts and opinions behind opioid therapy. The lack of knowledge about these medications and their appropriate use has often led to a deadly outcome. When used appropriately they can often help restore ones quality of life and function. The following course will cover a wide range of issues surrounding these medications and it is important that you complete it fully. There is an optional section after the course that I recommended you read as well. In order to establish that you have understood the information, you will be given a set of questions to answer. Upon completion of the course you will also be given a printable “Certification of Completion”. We recommend you provide a copy of this certification to your primary care physician and the physician prescribing your opioid medications.. The benefit to patients who use these drugs correctly can be tremendous. Therefore, it is vital that we understand and develop better and safer practices to protect both the patients and the community from the misuse of these medications or they will no longer be available in the future. As a community let us learn to USE the medications appropriately and not ABUSE them. You will notice a lot of repeated information in this website which was done intentionally to stress the importance of critical information.

Opioid therapy is not right for every patient, however for some this may be a reasonable option. You should always try non-opioid therapies before considering opioid therapy and understand the benefits, risk and alternative options before starting opioid therapy. Often our treatment plan will be combined with non-opioid therapies. It is important that you establish treatment goals to improve pain and function.

Patient undergoing opioid therapy are usually required to sign a treatment agreement with our provider. It is your responsibility to read your treatment agreement and informed consent before starting opioid therapy. These agreement usually stipulates that you will only receive opioid or other controlled medications from one provider/clinic. Often these will usually be in association with a monthly office visit for therapeutic drug monitor and appropriate medical supervision. You should always follow all office policies in your treatment agreement. Safety monitoring will usually include but not limit to routine urine drug screening and CURES monitoring. Only use medications as prescribed. You should NEVER take more than prescribed and taking more medications than prescribed increases the risk of significant adverse events such as death. You must lock up all your opioid medications in a safe.

**(PLEASE READ FULL DISCLAIMER AT END OF COURSE BEFORE PROCEEDING)**

“In 2008, nearly 36,500 Americans died from drug poisonings, and of these, nearly 14,800 deaths involved opioid analgesics.” --FDA

“Almost 16,000 Americans died of overdose involving opioids in 2009.” -- FDA

“In 2009, there were nearly 343,000 emergency department visits involving nonmedical use of opioid analgesics.” --FDA

“Based on the 2010 National Survey on Drug Use and Health, public health experts estimate more than 35 million Americans age 12 and older used an opioid analgesic for non-medical use some time in their life—an increase from about 30 million in 2002.” --FDA

“In 2011, an estimated 22.9 million prescriptions for extended-release and long-acting opioids were dispensed in the U.S.” -- FDA

“80% of the world's pain pills are consumed in the United States.” -- American Society of Interventional Pain Physicians.

“The total annual incremental cost of health care due to pain ranges from \$560 billion to \$635 billion (in 2010 dollars) in the United States, which combines the medical costs of pain care and the economic costs related to disability days and lost wages and productivity. In 2010 there were an estimated 100 million Americans dealing with chronic pain.” – AAPM

“Accidental overdoses from prescription drugs now exceed the combined total of deaths from heroin, crack and methamphetamines. Accidental deaths from overdoses resulting from legal prescription drugs now exceed deaths by car accidents.” – CNN

“Every 19 minutes someone dies from a drug overdose in the United States. This number includes those dying from both legal and illegal drugs; however, most are due to legal prescription drugs.” – Dr. Sanjay Gupta

“I just want people to remember: opioid addiction is a deadly disease, it kills people all the time, we are dealing with a fatal illness more likely to kill you than the vast, vast, vast majority of cancers—that’s a fact” – Dr. Drew Pinsky

“The medications don’t pull the trigger, but the failure to educate ourselves and our patients about the safe use of these medications is deadly.” – Dr. Yogi

## **(TERMINOLOGY)**

*(Picture: Terminology)*



First it is important that we understand some important terminology as we go forward with this program:

### **USE**

Using a medication as prescribed to treat an illness or symptom, i.e. such as opioid medications to treat pain. The use is in a manner that is safe both for the patient and the individuals around them. This also includes the safe storage and disposal of medications to prevent the accidental misuse of these medications by others.

### **ABUSE**

Abuse is the self-administration of medications to alter one's state of consciousness ("get high"). This is an intentional, maladaptive pattern of use of a medication (whether legitimately prescribed or not) leading to significant impairment or distress, such as repeated failure to fulfill role obligations, recurrent use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems, and usually occurring over a 12-month period.

### **MISUSE**

Misuse (noncompliant use) is the intentional or unintentional use of a prescribed medication in a manner that is contrary to directions, regardless of whether a harmful outcome occurs. Misuse can be grouped into several categories:

- Not taking the medication according to the prescription
- Unsanctioned use (running out early; bingeing)
- Altering the route of delivery (injecting, crushing tablets, snorting, chewing)

- Accessing drugs from other sources (friend, the street, other doctors)
- Drug-seeking behavior (anger, harassing office staff for fit-in appointments)
- Reluctance to use other methods of pain management

## **ILLCIT USE**

Non-medical use (prescription drug abuse, illicit use) is intentional or unintentional use of legitimately prescribed medication in an unprescribed manner for its psychic effect (either experimentation or recreationally). It also includes deciding to increase the dose of one's own medication, taking a larger dose than directed, engaging in a suicidal attempt or gesture, and inadvertent poisoning. The non-medical use of prescription medications implies that the person is using the drug for reasons other than those indicated in the prescribing literature or other off-label uses prescribed by a clinician. Nonmedical use includes procurement of drugs for abuse, bartering, suicide, homicide, or accidental ingestion.

## **DIVERSION**

Diversion: Redirection of a prescription drug from its lawful purpose to illicit use; can be done with criminal intent.

## **OPIOID-INDUCED HYPERALGESIA**

Opioid-induced hyperalgesia (OIH) is defined as a state of nociceptive sensitization caused by exposure to opioids. The condition is characterized by a paradoxical response whereby a patient receiving opioids for the treatment of pain could actually become more sensitive to certain painful stimuli. The type of pain experienced might be the same as the underlying pain or might be different from the original underlying pain. OIH appears to be a distinct, definable, and characteristic phenomenon that could explain loss of opioid efficacy in some patients. Opioid-induced hyperalgesia may develop as a result of long-term opioid use in the treatment of chronic pain. Various studies of humans and animals have demonstrated that primary or secondary hyperalgesia can develop in response to both chronic and acute exposure to opioids. This side effect can be severe enough to warrant discontinuation of opioid treatment.

## **PHYSICAL DEPENDENCE**

Physical dependence is a physiologic state of adaptation that often includes tolerance and is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood levels of the drug, and/or administration of an antagonist. Physical dependence involves the related phenomenon of withdrawal and tolerance.

### **TOLERANCE**

Tolerance is a state of adaptation in which repetitive exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. Tolerance is more pronounced for some effects than for others; tolerance occurs quickly to the effects on mood, itching, urinary retention, and respiratory depression, but occurs more slowly to the analgesia and other physical side effects. However, tolerance does not develop to constipation or miosis (the constriction of the pupil of the eye).

### **WITHDRAWAL**

Withdrawal is known as a variety of unpleasant symptoms that occur after use of a drug that the body has become physically dependent after it is reduced or stopped. Withdrawal symptoms are thought to increase the risk for relapse. The withdrawal symptoms for opiates include difficulty concentrating, irritability, anxiety, anger, sleep disturbance, craving, severe dysphoria, sweating, nausea, rhinorrhea, depression, severe fatigue, vomiting and pain. Slowly reducing the intake of opioids over days and weeks will reduce or eliminate the withdrawal symptoms. The speed and severity of withdrawal depends on the half-life of the opioid; heroin and morphine withdrawal occur more quickly and are more severe than methadone withdrawal, but methadone withdrawal takes longer. The acute withdrawal phase is often followed by a protracted phase of depression and insomnia that can last for months. The symptoms of opioid withdrawal can also be treated with other medications, such as clonidine and antidepressants, but they still have limited abilities to lessen the symptoms of withdrawal.

### **ADDICTION**

Addiction is a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Sometimes called "psychological dependence," addiction should not be confused with "physical dependence" (e.g., tolerance, withdrawal ) that may naturally occur with opioid analgesics.

### **(SAFETY)**

*(Picture: Safety)*



Opioid related deaths have been a hot topic recently as well as in the past. Their safety and role in the treatment of chronic diseases such as pain as come into question. However, studies over the past 20 years have repeatedly shown opioids to be safe when they are used correctly. Multiple studies in the United States and around the world have shown opioids to be a safe and effective treatment option. Risk of opioid therapy also includes physical dependence, tolerance, opioid induced hyperalgesia, and addiction.

Often the adverse events related with the use of opioid medications involve over use and often are due to the combination of other “sedative” agents such as alcohol, benzodiazepines, sleep medications and/or other sedative medications.

The key point is that yes opioids are safe when USED CORRECTLY but they can be deadly if ABUSED. Please note like any medication, significant side effects such as death have been reported in individuals who take their medications correctly. The KEY to being SAFE is understanding the medications you take. This is why this course is a necessary part for anyone taking these or similar medications. It is important that patients speak to their doctor if they have any questions or safety concerns before starting opioid therapy. Please note there is limited evidence as to the benefits of long-term opioid therapy.

It is impossible to tell which patients need low doses and which need high doses, so we recommend that all patients start on low doses, especially those who are new to these medications. Over time if needed your doctor can titrate the dose of the opioid medication to provide more effective pain relief, while minimizing adverse side effects. It is important to understand that the lowest dose needed for effective pain control is recommended. Higher doses do not translate into better pain relief in many cases. Rather than adding high doses of opioids to your treatment plan talk to your doctor about the addition of other treatment options, which are discussed later in this course.

Opioid analgesics themselves for the most part do not cause any specific organ toxicity, unlike many other drugs, such as NSAIDs, aspirin and acetaminophen. They are not associated with upper gastrointestinal bleeding and renal toxicity like long term NSAID use. However, we do



still recommend annual liver and renal function test from your primary care doctor for patients who are on long term chronic opioid therapy. The metabolism and excretion of these medications are affected greatly by the liver and kidneys. We will discuss more about the side effects of these medications and issues in patients with liver and renal disease later in this course.

When using combination opioid products containing acetaminophen, aspirin, or ibuprofen (such as Norco®, Vicodin® or Percocet®), the dose limiting toxicity is generally attributable to acetaminophen, aspirin, or ibuprofen respectively. The maximum amount of acetaminophen should be no more than 4 grams/day considering all combined acetaminophen in 24 hours. Using more than 4 g/day of acetaminophen can cause acute hepatic failure. Aspirin and ibuprofen have their own inherent toxicities, including but not limited to possible gastrointestinal bleeding, kidney dysfunction, hypertension, etc. Maximum daily dose of aspirin is 4grams/day. The maximum daily dose of ibuprofen is 3.2grams/day. For chronic daily use of combination medications I recommend you use the least amount needed and I do not recommend more than 50% of the daily maximum dose of these medications when used chronically (i.e. acetaminophen no more than 2 grams a day). Also if used on a chronic basis routine and annual blood work by your primary care physician is recommended which includes liver and renal function tests. It is important that you report any abnormal lab results to the doctor who prescribes you your opioid medications.

It is important for us to note here, regarding senior citizens, opioid use is associated with increased adverse effects such as "sedation, nausea, vomiting, constipation, urinary retention, and falls. As a result older adults taking opioids are at greater risk for injury. We will also revisit this topic at the end of the course.

Opioids are well accepted for the treatment of acute pain, such as post-operative pain. They have been extremely valuable in the treatment of terminal disease such as cancer as well as severe degenerative conditions such as rheumatoid arthritis. When used properly they have also found to be an important modality in the treatment of chronic pain. The field of pain management itself also evolved over the decades and now patients with chronic pain are often treated by board certified pain medicine specialists.

Current opioids such as methadone should only be prescribed after trying other opioids first due to the higher risk of adverse side effects. Safety concerns with methadone are due to its sometimes unpredictable pharmacodynamics and pharmacokinetics. Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Never ever take more than prescribed when it comes to Methadone, as it can seriously lead to overdose and death.

To improve safety always inform your doctor of any change in your health. Inform your doctor if you have or develop COPD, Pneumonia, CHF, sleep apnea, alcohol or substance abuse, are over 65 years of age, have history of or develop renal or hepatic dysfunction. These conditions

may potentiate opioid adverse effects and require close monitoring. Even low doses of opioids can lead to more risks than benefits with these conditions.

The basic DOs and DON'Ts of opioid safety are

DO:

- Read the Medication Guide
- Take your medicine exactly as prescribed
- Do store your medications safely and securely and keep them out of the reach of children, pets, and household members, to avoid risks from unintended exposure
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

DON'T:

- Do NOT give your medicine to others
- Do NOT take medicine unless it was prescribed for you
- Do NOT suddenly stop taking your medicine without talking to your healthcare provider, as this may result in withdrawal.
- Do NOT break, chew, crush, dissolve, or inject your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider who will refer to the product labeling to determine if it is appropriate to sprinkle the contents of a capsule on applesauce or administer via a feeding tube
- Do NOT drink alcohol while taking this medicine
- Do NOT share these medications, even if someone has the same symptoms as you.

Call 911 Or Your Local Emergency Service Right Away If:

- You take too much medicine
- You have trouble breathing, or shortness of breath
- A child has taken your medicine

### Tell Your Healthcare Provider:

- Your complete medical and family history, including any history of substance abuse or mental illness
- The cause, severity, and nature of your pain
- If the dose you are taking does not control your pain
- About any side effects you may be having
- About all the medicines you take, including over-the-counter medicines, vitamins, and dietary supplements
- Your treatment goals
- If you have underlying respiratory disease

Certain medical conditions such as sleep apnea, pneumonia, COPD, etc. can increase your risk of overdose and respiratory arrest when combined with opioid therapy. If you develop pneumonia you should inform your provider as you may need to consider a reduction of your dose. If you suspect you snore heavily or have day time sleepiness, it is important you discuss with your provider the option of a sleep study to evaluate for sleep apnea and possible use of a CPAP machine.

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### **(GOLDEN RULES NOT TO BREAK)**

As you have already learned opioid medications can improve ones quality of life but these medications are highly addictive and when used improperly can lead to serious consequences such as death. There there are a few GOLDEN RULES that most pain clinics and physicians will expect you to adhere to. Please discuss with your particular physician or pain clinic as to their strict office policies. You should always read fully the treatment agreement provided to you by your clinic. Failure to comply with your treatment agreement will place you at increased risk of adverse events with the use of opioid therapy, such as overdose and death and may subject you to discontinuation of opioid therapy as an option in your treatment plan.

### **DO NOT VIOLATE THE FOLLOWING GOLDEN RULES**

- 1) **NO EARLY REFILLS: NEVER TAKE MORE THAN PRESCRIBED. ALWAYS FOLLOW THE DIRECTIONS GIVEN TO YOU BY YOUR PROVIDER**

REGARDING YOUR MEDICATIONS AND THAT WRITTEN ON YOUR PRESCRIPTION BOTTLE. DISCUSS WITH YOUR PROVIDER WHAT YOUR OPTIONS ARE TO TREAT A PAIN FLARE, AS OVERTAKING YOUR MEDICATION DUE TO A PAIN FLARE MAY NOT BE CONSIDERED A VALID EXCUSE. YOU MAY BE SUBJECT TO RANDOM PILL COUNTS BY YOUR PROVIDER TO ENSURE YOU ARE NOT TAKING MORE THAN PRESCRIBED.

- 2) **CURES**: YOUR PROVIDER MAY CHECK THE DEA DATABASE REGULARLY WHICH LIST ALL OPIOID MEDICATIONS PRESCRIBED. YOUR TREATMENT AGREEMENT WILL USUALLY STATE THAT YOU CAN NOT FILL OUTPATIENT OPIOID MEDICATIONS FROM OTHER OUTSIDE PROVIDERS, SUCH AS DENTIST, EMERGENCY ROOM, SURGEONS, ETC.
- 3) **URINE DRUG SCREENING**: YOUR PROVIDER MAY CHECK URINE DRUG SCREENS TO MAKE SURE YOU ARE ONLY TAKING THE OPIOID MEDICATIONS PRESCRIBED TO YOU. NEVER TAKE A FRIEND'S MEDICATION. NEVER TAKE OLD MEDICATION EVEN IF WAS PRESCRIBED TO YOU IN THE PAST ULESS INSTRUCTED BY YOUR PROVIDER. IF YOU ARE PRESCRIBED AN OPIOID MEDICATION THAT DOES NOT SHOW UP IN A UDS YOU MAY BE REQUIRED TO PROVIDE AN EXPLANATION. IT COULD BE CONSIDERED A VIOLATION WITHOUT A REASONABLE EXPLANATION FOR THE NON-PRESENCE OF A PRESCRIBED MEDICATION.
- 4) **30 DAY REFILL POLICY**: YOU TYPICALLY ARE PROVIDED A PRESCRIPTION THAT IS TO BE USED OVER A 30 DAY PERIOD. THIS MAY VARY FROM CLINIC TO CLINIC AS SOME CLINICS WRITE ONLY 28 DAY SUPPLIES, SO BE AWARE OF HOW LONG THE PRESCRIPTION YOU ARE GIVEN IS EXPECTED TO LAST. IF FOR EXAMPLE YOU ARE GIVEN A 30 DAY SUPPLY OF MEDICATIONS, YOU ARE NOT ALLOWED TO CONSUME A 30 DAY SUPPLY OF MEDICATIONS WITHIN 28 OR 29 DAYS. DUE TO PHARMACY ISSUES AND OTHER FACTORS PATIENTS MAY PICK UP THEIR NEXT PRESCRIPTION ON DAY 28 OR 29. IF SO THE EXPECTATION IS THAT YOU DO NOT OPEN THE NEXT PRESCRIPTION BOTTLE UNTIL DUE ("DAY 31"). YOU ARE RESPONSIBLE FOR KEEPING TRACK OF WHEN YOUR NEXT PRESCRIPTION IS DUE AND WHEN YOUR NEXT BOTTLE CAN BE OPENED. FAILURE TO COMPLY AND KEEP TRACK OF WHEN YOU CAN START YOUR NEXT PRESCRIPTION BOTTLE MAY BE CONSIDERED A VIOLATION YOUR TREATMENT AGREEMENT. YOU MAY BE REQUIRED BY YOUR PROVIDER TO BRING YOUR PRESCRIPTION BOTTLES TO EACH VISIT TO ENSURE COMPLIANCE.

## (PATIENT ASSESSMENT)

(Picture: Patient Assessment)



Opioid therapy is not right for everyone. Your doctor will determine after taking a thorough physical and medical history if the use of opioid therapy is an appropriate option to add to your treatment plan.

Opioid therapy should never be the only treatment option used to treat your pain. The use of adjuvant therapies and non-drug therapies are important parts of a successful treatment plan.

When it comes to opioid therapy, proper patient selection is critical. Your doctor will consider a trial of chronic opioid therapy only when potential benefits are likely to outweigh risks.

Before the trial you may be asked to sign a treatment agreement with your physician that will outline the expectations, safe use and office policies with regards to your treatment plan with or without opioid therapy. It is important that you read and understand these contracts fully.

In patients who experience mild or moderate opioid-related adverse effects, a longer trial may be indicated, because some adverse effects diminish with longer exposure. Some adverse effects can be managed with additional therapies (e.g., a bowel regimen for prevention or treatment of constipation).

Your physician will also ask you a multiple of questions to help determine the benefits and risks of opioids in your treatment plan. Studies have shown that the list of risk factors below are associated with a higher risk of opioid addiction and misuse.

<b>FACTORS ASSOCIATED WITH HIGHER RISK OF OPIOID MISUSE</b>
History of Substance Abuse
History of Alcohol Abuse

Family History of Substance Abuse
History of DUIs
History of Lost or Stolen Prescriptions
Use of Supplemental Sources to Obtain Opioids
History of Psychiatric or Psychological Disorders
History of Sexual Abuse During Childhood
Male Sex
Younger Age

It is important for you to provide your physicians with an accurate history and inform them if you have any of the above risk factors, as this is necessary for the delivery of safe care.

Research indicates that many forms of chronic pain can respond to chronic opioid therapy, although there is little evidence that opioids are effective when there is a strong untreated psychological component to the pain.

Before starting opioid therapy your physician may send you for a consultation with a pain psychologist. Psychological assessment is important when initiating therapy. It offers one promising avenue to detecting and balancing the risks of opioid therapy.

Safety is the biggest priority with the use of opioids for chronic pain management. The CDC and Medical Board of California both recommend patients with an above-average risk also consider a consult with a specialist in addiction medicine or similar specialty. It is typically performed twice a year. Factors that place patients at above-average risk include but are not limited to: higher than average doses of opioid medications, co-use with benzodiazepines or sedative medications, inconsistent CURES or UDS, Risk Evaluation (ORT) scores >3, etc.

Your physician may use the aid of a screening instrument when trying to determine if opioid therapy would be appropriate. Several screening tools have been extensively validated and include: the Screener and Opioid Assessment for Patients with Pain (SOAPP) Version 1, the revised SOAPP (SOAPP-R), the Opioid Risk Tool (ORT), and the Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument. It is important to be truthful during the screening process.

For all patients starting on opioid therapy, the treatment plan must be individualized. Initial use of opioids should be viewed as a short-term therapeutic trial lasting several weeks to several months. The decision to continue chronic opioid therapy after this period should be based on outcomes during the trial. Your physician will evaluate you for the degree of analgesia, improvement in activities and goals, degree of adverse effects, and signs of aberrant drug-related behaviors.

You should always set realistic expectations, and your physicians will work with you to develop SMART goals: Specific, Measurable, Achievable, Relevant, and Time-bound goals. For example, setting a concrete goal of being able to walk 20 minutes a day, 3 days a week by the next clinic visit is much more attainable than the goal “to feel like I did when I was 20 years old”.

Your provider will be looking for 5 main criteria to determine that you are benefiting from opioid therapy. This is often referred to as the “5As Of Opioid Therapy”. The medications should provide you Analgesia (pain relief), cause minimal Adverse side effects, improve your ADL (activities of daily living) and function, evaluate that you have good Affect (mood), and make sure you are not showing any Aberrant behavior such as overuse or abuse of your medications.

You should always attempt to understand your underlying diagnosis and chronic conditions.. For example chronic migraine sufferers should be able to explain to others what a migraine is. Knowledge is power and the more you know about your condition the better you will do. It is not uncommon for provider to give some of their patients “homework”, in the form of essay writing, when they feel it is necessary for them to obtain additional education about their underlying conditions.

Two important areas to discuss with your doctor with regards to your initial assessment of opioid therapy are any sleep disturbances and/or history of anxiety and/or depression. These three comorbid disease often are very common with chronic pain. Not only can they make chronic pain worse, chronic pain can increase the risk of developing these comorbid disease and turn into a vicious cycle. Thus it is important to together develop a treatment plan that will address these issues in addition to the treatment plan created to address your pain. If you ever develop suicidal thoughts or ideas it is important to immediately notify your provider or go to the nearest hospital.

## **(PAIN RELIEF VS FUNCTION/ADL)**

*(Picture: Pain Relief vs Function/ADL)*



Your doctor may often ask about changes in your function along with changes in your pain scores throughout your treatment.

They may ask you questions in regards to your activities of daily living (ADLs). Activities of daily living is a term used in healthcare to refer to daily self-care activities within an individual's place of residence and/or their outdoor environments.

Often patients may report no improvement in pain scores, but when questioned further they will show a significant improvement in function due to the treatments they received. As a patient it is important to evaluate yourself for improvement in function and not just improvement in pain.

Increase function can be a goal to focus on when deciding on treatment options to improve your overall quality of life. Having goals relating to increase in function can create more structure to one's management and justification for use of medications and treatments. Goals that you set should be simple and reasonable, such as being able to complete a favorite hike, being able to take one's grandchildren fishing, etc.

## **(ADJUVANT THERAPIES)**

*(PICTURE: Adjuvant Therapies)*





Adjuvant medications and therapies are medications and treatments used to help treat pain that are often used alone or in conjunction with opioid therapy.

It is important to understand that these medications and treatments exist and talk to your doctor about adding these therapies, if they are not part of your pain regimen. When used in conjunction with opioid therapy they have shown to reduce the amount of opioid medications needed and decrease the risk of tolerance.

Only you and your doctor together can determine which medications and other treatment therapies are appropriate for you to help treat your medical condition.

You should empower yourself by educating yourself not only about your medical condition but also about your medications and treatment options available to manage your condition.

When it comes to pain management there is a wide variety of medication categories in addition to opioids used to treat pain. These include but not limited to:

- 1) NSAIDS
- 2) Oral Steroids
- 3) Acetaminophen
- 4) Anticonvulsants
- 5) Muscle Relaxants
- 6) Antidepressants
- 7) Anti-Rheumatics
- 8) Migraine Medications
- 9) Dopamine Stimulants
- 10) Gout Medications
- 11) Medications to treat side effects such as: Constipation and Nausea

Not all of the above medications are appropriate for everyone, and they too come with their own risk and side effects.

In the MyPainTools tutorial you learned that there are many different types of underlying pains such as nociceptive and neuropathic pain.

Neuropathic pain often is treated best with medications that target that particular pain mechanism such as with anticonvulsants and antidepressants, often referred to as “neuropathic” medications.

Acute and/or inflammatory pain, that is often nociceptive, can often be managed with short term anti-inflammatory medications.

Often interventional procedures you might receive to help you manage your pain may include a steroid epidural injection which is a strong anti-inflammatory medication.

It is important to include in your treatment plan interventional treatment options as well as alternative and integrated medicine such as acupuncture.

By now you already know that opioid medications have the known risk of tolerance and we recommend rather than increasing your opioid medications when you have a pain flare, you strongly consider the use of adjuvant medications or therapies discussed above. These therapies can help decrease your pain back and avoid the need for increasing doses of opioid medications.

## **(MEDICATION SIDE EFFECTS)**

*(Picture: Medication Side Effects)*



Like all medications opioids can have side effects. You should always read the Medication Guide you receive from your pharmacist each time a medication is dispensed to you. Report any side effects or changes in your health to your physician so they can make appropriate changes as needed. Likewise, report any change in your health or any comorbid diseases you have or

develop as this can affect your doctor's decision when determining your treatment plan. Failure to do so can lead to unexpected side effects including overdose and death.

There are 4 absolute contraindications to the use of opioid therapy:

- 1) Significant respiratory depression
- 2) Acute or severe chronic bronchial asthma
- 3) Known or suspected paralytic ileus
- 4) Hypersensitivity to the medication

Use caution in patients with:

- 1) Biliary Colic
- 2) Head Injury
- 3) Reduced Blood Volume
- 4) Severe Hepatic Insufficiency
- 5) Convulsion states

Some important opioid-related adverse effects to report to your physician include things such as constipation, nausea, worsening pulmonary disease, sedation, and cognitive impairment. Inform your provider immediately if you develop pneumonia or other lung diseases as it may be necessary to lower your opioid doses during this time due to risk of overdose even if you are taking your normal doses as prescribed. Recent research indicates that chronic opioid therapy is associated with a high frequency of sleep-disordered breathing, suggesting cautious use in patients with sleep apnea. If you suspect that you have sleep apnea, have day time tiredness or have excessive snoring you should ask your doctor for a sleep study. If you know you have sleep apnea please inform your doctor and consider treatment such as with a CPAP machine. Failure to take the necessary steps such as the use of a CPAP if you have sleep apnea can increase your risk of overdose and death. In patients with underlying cognitive impairment, chronic opioid therapy may increase the risk of falls or delirium. Opioid-related constipation is likely to be particularly problematic in patients with pre-existing constipation. Among opioids, fentanyl is probably least likely to cause constipation, but there is considerable variation among patients; therefore, opioid rotation may be considered for refractory constipation.

Some of the side effects of opioids are secondary to histamine release from mast cells, such as itching and facial flushing.

Common adverse reactions in patients taking opioids for pain relief include: nausea and vomiting, drowsiness, itching, dry mouth, miosis, and constipation.

Note dry mouth can lead to cavities and other dental issues, so it is important that if you are on chronic opioid therapy that you see a dentist regularly. Some opioids medications contain sugar and increase this risk if used chronically.

Other adverse reactions in patients taking opioids for pain relief include: dose-related respiratory depression, confusion, hallucinations, delirium, urticaria, hypothermia, bradycardia/tachycardia, orthostatic hypotension, dizziness, headache, urinary retention, ureteric or biliary spasm, muscle rigidity, myoclonus (with high doses), flushing (due to histamine release), mood swings, weight gain, depression, osteoporosis, chronic fatigue, sexual dysfunction. Both therapeutic and chronic use of opioids can compromise the function of the immune system. However the relevance of this in the context of pain relief is not known.

Men who are taking moderate to high doses of an opioid analgesic long-term are likely to have subnormal testosterone levels, which can lead to osteoporosis and decreased muscle strength if left untreated. Serum levels of testosterone and estradiol are associated with an increased risk of osteoporosis. If you are on opioid therapy you should discuss with your primary care physician if testing your testosterone level during your annual physical is reasonable and if treatment if appropriate. Patients getting testosterone replacement therapy should have prostate-specific antigen levels monitored as there is a risk of prostate cancer with this therapy and you should consult with your primary care physician before starting testosterone replacement therapy.

## **OPIOID AFFECTS ON THE BODIES ORGAN SYSTEMS**

### **CENTRAL NERVOUS SYSTEM**

- 1) Analgesia
- 2) Sedation
- 3) Euphoria/Hallucinations
- 4) Mental Clouding
- 5) Respiratory Depression
- 6) Nausea and Vomiting
- 7) Suppresses Cough Reflex
- 8) Miosis (small pupils)

### **GASTROINTESTINAL TRACT**

- 1) Decrease GI Motility
- 2) Increase GI Tone
- 3) Constipation
- 4) GI Spasms

- 5) Biliary Tract Spasms

#### CARDIOVASCULAR

- 1) Bradycardia at high doses
- 2) Orthostatic Hypotension
- 3) Peripheral Vasodilation (Histamine Effect)
- 4) Itching (Histamine Effect)

#### URINARY TRACT

- 1) Urinary Retention
- 2) Increased Urinary Sphincter
- 3) Decrease Urine Production

#### UTERUS

- 1) Prolongs Duration of Labor

#### BRONCHIAL SMOOTH MUSCLE

- 1) Bronchoconstriction (Histamine Effect)

#### ENDOCRINE SYSTEM

- 1) Decrease Release of ACTH, Prolactin, and Gonadotrophic Hormones (Testosterone)

#### MUSCULOSKELETAL SYSTEM

- 1) Muscle Rigidity (High Doses)

#### IMMUNE SYSTEM

- 1) Suppression of Immune System (chronic use)

#### PREGNACY (see opioids and pregnancy section below)

- 1) All Opioids cross the placenta
- 2) Neonatal Withdrawal Syndrome

#### (MANAGING ADVERSE EFFECTS)

**Nausea and Vomiting:** tolerance occurs within 7–10 days, during which anti-emetics can be very effective. The following are the most commonly used anti-emetics:

- 1) Zofran®
- 2) Reglan®
- 3) Compazine®
- 4) Phenergan®
- 5) Hydroxyzine
- 6) Benadryl®

**Drowsiness:** tolerance usually develops over 5–7 days, but if troublesome, switching to an alternative opioid often helps.

Certain opioids such as fentanyl, morphine and diamorphine tend to be particularly sedating, while others such as oxycodone, and meperidine (Demerol®) tend to produce comparatively less sedation, but individual patients responses can vary markedly and some degree of trial and error may be needed to find the most suitable drug for a particular patient. Although in some case CNS stimulants can be helpful we recommend avoiding the use of stimulants due to cardiovascular adverse events. Increased aerobic exercises to your daily routine will also help with reducing the level of drowsiness.

**Itching:** Does not tend to be a severe problem when opioids are used for pain relief, but when required, antihistamines are useful. Non-sedating antihistamines such as Allegra® are preferable so as to avoid increasing opioid induced drowsiness. Other drugs that can be used to treat the side effects of itching include:

- 1) Allegra®
- 2) Norflex®
- 3) Claritin®
- 4) Phenergan®
- 5) Cyclizine®
- 6) Benadryl®

**Constipation:** develops in many people on opioids and since tolerance to this problem does not develop readily, most patients on long-term opioids will need specific treatment.

Mild/Moderate Constipation:

- 1) For mild cases, increase water intake (around 1.5 L/day), use fiber and colace and consider drinking prune juice.
- 2) If needed the addition to the laxative and stool-softeners can be considered (e.g. Docusate® in combination with Bisacodyl® or Senna®)(many question the benefit of stool-softeners long term)
- 3) Peripherally-acting opioid antagonists (e.g. methylnaltrexone) effectively prevent constipation while not affecting centrally mediated analgesia or provoking withdrawal syndrome, however these can still potentially reduce the efficacy of opioid analgesics in the treatment of conditions where much of the pain relief comes from action at peripherally situated opioid receptors, such as in inflammatory conditions like arthritis or post-surgical pain.

#### Severe Constipation/Chronic Cases:

For more severe and/or chronic cases, the drugs that are used work by not increasing peristalsis, but by preventing water uptake in the intestine, leading to a softer stool with a larger component of water, and, additionally, by acidifying the environment inside the intestine, which both decreases water uptake and enhances peristalsis (e.g. lactulose, which is controversially noted as a possible probiotic). The following drugs are generally efficacious:

- 1) Polyethylene glycol 3350 (MiraLax®, GlycoLax®).
- 2) Lactulose® syrup

Always consult your doctor as long term use of laxatives is not recommended and can have its own side effects.

#### Other Options:

One combination, oxycodone/naloxone, aims to reduce systemic side effects by combining oxycodone with an opioid suppressor, naloxone, in a form which does not pass through the blood–brain barrier. Thus, the constipation effect is suppressed, but not the pain reduction.

Peripherally acting opioid antagonists such as methylnaltrexone (Relistor®) have been found to effectively relieve opioid induced constipation without triggering withdrawal symptoms.

There are many advertised natural alternatives and recipes available on the internet to treat constipation. Some have a good long term track record, but other may not. So if you explore these options be sure to consult with your doctor as to the safety issues with these alternative therapies.

**Respiratory depression:** although this is the most serious adverse reaction associated with opioid use it usually is seen with the use of a single, intravenous dose in an opioid-naïve patient. In patients taking opioids regularly for pain relief, tolerance to respiratory depression occurs rapidly. Respiratory depression is not a clinical problem normally when medications are only taken as prescribed and not mixed with other sedative drugs. Several drugs have been developed which can partially block respiratory depression, although the only respiratory stimulant currently approved for this purpose is doxapram, which has only limited efficacy in this application. Please note opioid therapy is contraindicated for patient with severe respiratory depression. If you have any concerns or issues with respiratory depression call your physician immediately or dial 911.

## (ONGOING THERAPY AND MONITORING)

*(Picture: Ongoing Therapy and Monitoring)*



The Medical Board of California (MBC) has created guidelines and recommendations to help patients and providers safely prescribe and use opioid therapy to improve the quality of life of patients., while preventing drug diversion and abuse. You will also be responsible to abide by the MBC guidelines and all DEA, state and federal regulations.

Before prescribing you medications your physician will perform a complete medical history and physical examination. This will include an assessment of your pain; your physical and



psychological function; a substance abuse history; history of prior pain treatment; an assessment of underlying or coexisting diseases or conditions; and documentation of the presence of a recognized medical indication for the use of a controlled substance. It is important that you be honest and provide as much information as possible to your physician. You must have a reasonable medical need and indication to be prescribed opioid therapy to manage your pain. As stated before at your initial visit it is your responsibility to bring to your doctor's appointment your past medication records, including any lab or imaging studies and a list of your current and past medications as well as the original bottles.

During your follow up visits your physician will be looking for objectives by which the treatment plan can be evaluated, such as pain relief and/or improved physical and psychosocial function, and indicate if any further diagnostic evaluations or other treatments are needed. Your physician will tailor pharmacological therapy to your individual medical needs. Multiple treatment modalities and/or a rehabilitation program may be necessary if your pain is complex or is associated with physical and psychosocial impairment. It is important that you not only focus on your "pain scores" but also on your improvement in physical and psychosocial function when discussing your care with your physician.

Your physician will also review the risks and benefits of the use of controlled substances and other treatment modalities with you (most of which is provided in this tutorial). It is your responsibility to ask questions and ask for this information as well.

The physician will periodically review the course of your pain treatment and any new information about the etiology of your pain and the state of your health. If your progress is unsatisfactory, your physician may assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

Your physician may consider referring you to other specialist as necessary for additional evaluation and treatment in order to achieve treatment objectives.

To comply with DEA, state and federal recommendations your physician will require certain additional safe guards when prescribing controlled substances such as opioid medications. These guidelines and recommendations were developed to provide increased safety when using opioids as part of your treatment plan. Failure or refusal to comply with these recommendations can be a reason why your physician may determine that opioid therapy is not an appropriate option as part of your treatment plan.

To overcome the critical challenge of eliminating or significantly curtailing abuse of controlled prescription drugs and at the same time assuring the appropriate treatment for patients who can be helped by these medications, you may be required to comply with opioid therapy monitoring programs.

One of these safe guards used to monitor opioid therapy is routine urine drug screening known as UDS testing. Urine drug testing is a widely used and familiar method for monitoring opioid use in chronic pain patients. Urine drug testing can help track patient compliance and help decrease the risk of drug misuse and abuse, thus increasing safety with the use of opioid therapy.

Another monitoring tool during opioid therapy that your physician may use includes a state specific Prescription Monitoring Program. For example this program in California is called: Controlled Substance Utilization Review and Evaluation System (CURES), which is part of the California Prescription Drug Monitoring Program (PDMP). As of 2013 there is no federal database so most states have developed their own prescription monitoring program.

Each State Department of Justice, has a Prescription Drug Monitoring Program (PDMP) system which allows pre-registered users including licensed healthcare prescribers eligible to prescribe controlled substances, pharmacists authorized to dispense controlled substances, law enforcement, and regulatory boards to access timely patient controlled substance history information. By having access to controlled substance history information at the point of care it will help your physician make better prescribing decisions and cut down on prescription drug abuse. It allows physicians to see all the controlled prescriptions you have been prescribed and by whom to ensure you are only getting opioid therapy from one provider/clinic.

The online PDMP system will make it much easier for physicians and pharmacists to quickly review controlled substance information via the automated Patient Activity Report (PAR) in an effort to identify and deter drug abuse and diversion through accurate and rapid tracking of Schedule II through IV controlled substances. This is an important added safety measure to help assure the safe use of these medications as part of your treatment plan.

To ensure your safety and compliance with opioid therapy your physician may also perform random pill counts. It is important that you comply with these random pill counts. Some physician will require patient to bring with them their pain medications in their original bottles to each office visit.

Another part of ongoing therapy and monitoring is routine blood work. If you take chronic opioid medications you should ask your primary care physician to include in your annual check-up liver and renal function test. You should also report to your provider if you develop any heart or lung disease or worsening of organ function as this can have an adverse effect on your health. Your doctor may also ask for annual EKGs. For example if you take methadone you should also include annual EKGs due to risk of QTc prolongation and cardiac arrhythmias.

## **(MEDICATION SAFE STORAGE AND DISPOSAL)**

*(Picture: Medication Safe Storage and Disposal 1 & 2)*



The majority of people abusing prescription opioids for non-medical reasons often obtain them from friends or family members, often without their consent.

It is important and your responsibility to keep your opioid medication stored in a safe, secure, dry place, where a pet, child, teenager, family member, or stranger cannot get to them.

Do not store your opioids medications in several different locations around the home. You should keep the tablets in a bottle with a child-resistant lid, and keep the bottle in a secure lockbox that is approved by your doctor. Only you, and if needed your caregiver, should have access to the lockbox. If you suspect another person may be stealing your medications please inform your physician, this includes family member and/or your caregiver.

When disposing of opioid therapies there are certain guidelines you should follow. Remember expired and unused opioid medication should never be saved. If you receive prescriptions for a different dose of your current medications or you receive prescriptions for new medications, you must safely dispose of the leftover old medications. You should never take old opioid medications or medications that have been discontinued as part of your treatment.

You should consult the medication guide that accompanied your prescriptions for tips on safe disposal specific to your medication, and also follow the instructions given to you by your physician or pharmacist.

As far as actual physical disposal of your unused meds, some opioid medications can be flushed down the toilet; other kinds should be broken up and mixed with coffee grounds or cat litter prior to being thrown away (this makes the medication less tempting to children or pets and unrecognizable to people who may intentionally search through your trash). Before flushing your medications (for those that can safely be disposed of in this manner), you should contact your local water treatment or sanitation department to see if your community has restrictions regarding flushing medicines down the toilet and to find out how to safely dispose of medicines

in your community. Before discarding empty pill bottles, you should also remove all labeling to protect your identity.

The FDA offers several good resources that offer detailed information and instructions about how to properly dispose of prescription pain medications,. You can obtain this information by clicking on: [“Disposal of Unused Medicines: What You Should Know”](#). This website features a list of medications recommended for disposal by flushing.

The Drug Take-Back Network website offers information about “strategies already underway to reduce drug abuse and accidental poisonings, and to improve water quality by offering consumers a safe option for disposing of their unused drugs. Visitors to the site will find links to information about permanent and/or regularly recurring programs to collect and dispose of unused medications in 22 states. The site also includes a link to a national directory (searchable by ZIP code) of “one-time, occasional, or on-going take back programs. Click here for more information: [The Drug Take-Back Network](#).

Speak to your prescribing physician or pharmacist with regards to their medication take back policies as well.

## **(DISCONTINUING OPIOID THERAPY)**

*(Picture: Discontinuing Opioid Therapy)*



Just as starting and maintaining opioid therapy should be done with caution and only under the supervision of a trained professional, so should the discontinuation of opioid therapy. Always consult with your doctor so together you can develop a plan to safely and effectively discontinue opioids.

If at any point the risk outweighs the benefits for you to continue opioid therapy we will provide you a discontinuation plan that typically involves a slow titration off opioid therapy by approximately 10% per week.

There are several reasons to discontinue chronic opioid therapy for a patient who has been receiving opioids for management of a chronic pain condition. These include medication side effects, patients wish to discontinue opioid therapy, loss of meaningful clinical benefit from the medications, misuse or concerns regarding adherence to the treatment agreement and office policies, reduction in one's pain no longer requiring opioid therapy, and as well as changes in one's health resulting in opioid therapy being more harmful than beneficial.

Opioid rotation is an alternative to discontinuation. Patients may be wary to try another agent or may experience intolerable adverse effects with certain chemical classes of opioids. Often, implementing an "exit" strategy will involve tapering the opioid that you are taking.

Weaning from opioids can be done safely by slowly tapering the opioid dose and considering several other factors. As each individual is different your doctor will tailor a tapering plan based on your needs. An accepted rule of thumb for the safe and slow taper of opioid therapy is reduction of your current dose by 10% each week.

Keep in mind that some patients can be tapered more rapidly without problems. You should not suddenly discontinue opioid therapy due to risk of withdrawal. Opioid withdrawal syndrome may be encountered and be unpleasant, but it is typically not medically serious. Please note here that although withdrawal from opioids is not considered lethal, significant withdrawal from benzodiazepines and alcohol can be deadly. Also when deciding to discontinue Soma®, you must also titrate off slowly as significant withdrawal is possible.

It is normal to have concerns about tapering off long acting opioid medications due to fear and anxiety of increased pain or development of withdrawal symptoms. Typically, the last stage of tapering is the most difficult. Usually the initial tapering is well tolerated and the most difficult period of titration is when titrating off the last 30-50mg of morphine equivalents. Opioid withdrawal is typically not dangerous, but it may cause considerable discomfort.

It is important to understand and recognize the symptoms of withdrawal if you experience them and inform your doctor of these side effects.

Symptoms of opioid withdrawal include but not limited to: nausea, vomiting, increased heart rate, anxiety, abdominal cramps, diaphoresis, diarrhea, dilated pupils, increased respiratory rate,

runny nose, muscle spasms and twitching, muscle and body aches, goose bumps, increased blood pressure, insomnia, and/or lacrimation.

Consult your physicians on treatment options if needed to address withdrawal symptoms. Symptoms such as hypertension, cramps, nausea, diarrhea, muscle pain, diaphoresis, tachycardia, and myoclonus, can be managed with alpha-2 adrenergic agents, such as Clonidine, during the taper while monitoring for hypotension and anticholinergic side effects. Clonidine is not FDA-approved for this use, although evidence supports use in this setting. Group Health recommends clonidine as the first-line agent, as it is effective in many patients. Regular monitoring of blood pressure and pulse are needed. Dosing of clonidine depends on whether patient is acutely withdrawing or gradually being tapered. These are high-risk medications for the elderly.

Antihistamines or trazodone® may be used to help with insomnia and restlessness. Nonsteroidal anti-inflammatory agents may be used for muscle aches, and Imodium® for diarrhea. It is important to note that symptoms of mild opioid withdrawal may be present for up to 6 months after opioid discontinuation.

Other medications used to treat subjective symptoms during acute withdrawal and/or gradual taper include Hydroxyzine 25-50 mg every 6 hours as needed for anxiety, restlessness and insomnia. Diphenhydramine 25-50 mg every 6 hours as needed for itchiness. Promethazine 25 mg every 6 hours or Metoclopramide 10 mg every 6 hours as needed for nausea. Calcium carbonate (Tums®) 500 mg 1–2 tabs every 8 hours as needed for dyspepsia. Mylanta® or Milk of Magnesia® (follow package instructions) may also be used for dyspepsia. Acetaminophen (Tylenol®) 325 mg every 4-6 hours as needed for fever (not to exceed 2-3 g/24 hours, and also note that some narcotic medications already contain acetaminophen. (Always consult your own physician before taking or starting any new medications.)

Often slowing the taper rate can decrease the withdrawal symptoms. Your physician may also consider the use of benzodiazepines, such as Valium®, to help overcome withdrawal symptoms; however these medications should also be used with caution due to their inherent side effects and addiction concerns and only should be used under the supervision of a trained specialist familiar with these medications.

Your physician may also seek the help of a specialist such as an addictionologist should the need arise and it will be important for you to follow these recommendations. If a monitored outpatient tapering (i.e. detoxification) program is not appropriate your doctor will refer you to an inpatient detoxification program or a more advanced outpatient detoxification program.

During this time it is important to continue or add non-opioid management treatment strategies. These can include non-opioid pharmacologic therapies; invasive treatments as appropriate (e.g., epidurals, trigger point injections, spinal stimulator); rehabilitative strategies (e.g., physical therapy); cognitive behavioral approaches (e.g., biofeedback), etc.

Keep in mind that discontinuing opioids is not the same as discontinuing pain management, and your physician will work with you to develop additional treatment options to better help control your pain.

Patients with a long history of taking chronic opioids or any centrally acting medications such as dopamine agonists and SSRIs are more likely to experience withdrawal from a taper that is too rapid, and therefore may require a longer taper period to avoid such symptoms.

Your physician may consider the use of methadone as the drug of choice for the tapering process. Methadone is less likely to produce euphoria and is inexpensive compared with the other long-acting agents. It must be made clear however that the methadone is being used to treat pain, and that the taper is being done for medical reasons, not for substance abuse rehabilitation.

People taking short acting medications such as morphine, hydromorphone, or oxycodone may experience withdrawal symptoms within 6 to 12 hours of the last dose while those taking methadone or controlled-release opioids will experience symptoms typically 1 to 4 days after the last dose. Withdrawal from morphine typically lasts 5 to 10 days, while withdrawal from methadone or other long-acting opioids lasts longer. Often the first three days of withdrawal are the most intense and over time these symptoms will normally improve.

It is important that during the tapering process that you never break or open the medications, or cut the patches. This can release the entire dose at once, causing overdose and possible death. Instead your doctor will recommend you take the whole tablet or capsule or use the whole patch, but take or use the medication less often to reduce the dosage.

Drink a lot of fluid, try to stay calm, and keep reassuring yourself that the withdrawal reaction will pass and you will eventually feel better. One of the symptoms during opioid withdrawal is a state of sensitized pain, meaning your pain may feel more intense or severe. This also will pass with time.

Remember: Always seek professional healthcare assistance as soon as you can, if possible, before running out of medication.

## **(CO-USE WITH BENZODIAZEPINES AND ALCOHOL)**

*(Picture: Co-Use with Benzodiazepines and Alcohol)*



Benzodiazepines and opioid medications are used concomitantly in various circumstances, for example in anesthesiology, for the management of acute or chronic pain and for substitution therapy. Please note here that many of the same learning points and concerns in this tutorial with regards to opioid therapy also apply to the use of benzodiazepines.

Please note we do not recommend you consume alcohol while on opioid therapy. We also strongly recommend you do not start benzodiazepines. Also consider talking to your PCP about discontinuing any benzodiazepine therapy if possible. Alcohol, benzodiazepines as well as sleep medications such as Ambien when combined with opioid therapy increase your risk of respiratory depression and death. The FDA has release a black box warning with regards to the co-use of opioids and benzodiazepines (such as valium, Xanax, Clonazepam) which can lead to accidental overdose and death.

It is important to try to find alternative options in place of benzodiazepines when also under opioid therapy. You should also consider a consultation with a psychiatrist or sleep specialist if needed to determine if there are more effective and safer options to address issues with anxiety and insomnia. Just as with any medications the lowest doses needed should be used and side effects should always be reported to your physician.

As with co-use of benzodiazepine with opioid therapy the use of alcohol while undergoing opioid therapy also increases the risk of side effects and increases your risk of over dose and death.

The combination of alcohol and opioids can be deadly, and leads to hundreds of accidental overdoses each year. Mixing alcohol with opioids causes severe respiratory problems and cardiac arrest among other numerous health concerns. If you take opioid medications regularly, you are at risk for dangerous drug interactions every time you take a drink.

We strongly recommend patients do not combine alcohol use while on opioid therapy. The excessive use of alcohol is an absolute contraindication to the use of opioid therapy. If you are



consuming alcohol or feel you have a drinking problem please inform your physician immediately.

Patients often wonder if a small consumption of alcohol while on pain medications, such as a glass of wine with dinner is safe? This is a difficult question to answer due to individual differences between patients, and it is impossible to know in advance how much is “too much” alcohol. Concerning symptoms that you should watch out for include drowsiness, confusion, or dizziness. If you experience these side effects seek medical care immediately. Again we strongly recommend you do not consume any form or any amount alcohol while taking opioid medications as well as if you are taking benzodiazepines. Benzodiazepines combined with alcohol with or without opioid medications have similar serious concerns for overdose and death and should be avoided.

### **(DRIVING AND OPIOIDS)**

*(Picture: Driving and Opioids)*



It is important that when you first start opioid medications or have a change in the dose of your medication that you avoid driving an automobile or operate potentially dangerous equipment. This is for your own safety as well as to protect other persons. Until your body becomes accustomed to the opioids you may feel sleepy, less alert, and have slower reaction times, which can result in serious accidents.

It is important to remember that you may have poorer ability to drive or perform other tasks that require attention and skill even if you do not feel sleepy or otherwise different.

Depending upon your state of residence, it may be illegal for you to drive at all even when you take a medically recommended dose of prescription painkillers. As laws can change over time please consult with your state government's website to understand the laws governing driving while on prescription medications, such as opioid therapy. It is your responsibility to be up-to-

date on the DEA, state and federal regulations and guidelines and lack of knowledge is not accepted as an excuse by government agencies.

It is ALWAYS illegal to drive while impaired by any substance including opioids and benzodiazepines in ALL states.

Currently as of 2013 there are 15 states in which driving with any amount of an impairing drug, include prescription opioids, is illegal: Arizona, Georgia, Indiana, Illinois, Iowa, Michigan, Minnesota, Nevada, North Carolina, Ohio, Pennsylvania, Rhode Island, Utah, Virginia and Wisconsin. Keep in mind that even if you didn't take your painkiller that day, you likely still have remnants of the opioids in your bloodstream. The presence of such metabolites in your body could lead to a driving or operating while intoxicated charge in these states, according to the NIDA. Check your state government website for further details and regulations.

California also has some particularly strict laws when it comes to "drugged driving," according to the unofficial DMV Guide. The law does not distinguish between illegal drugs, opioid prescription drugs, alcohol and even over-the-counter remedies. Even driving after taking an over-the-counter medication, that causes drowsiness, could result in a driving under the influence (DUI) or driving while intoxicated (DWI) charge if the police officer feels you are impaired, even if you have a legal prescription. Always error on the side of safety and use caution with any medication, especially opioids when driving. Please note it is illegal and unsafe to drive or operate heavy machinery while impaired.

## **(OPIOID OVERDOSE TREATMENT)**

### **SUSPECTED OPIOID OVERDOSE TREATMENT**

With the rise in concern for opioid deaths due to overdose and rise in opioid prescriptions over the years, the CDC has recommend that physicians prescribe take-home emergency treatments such as Naloxone for opioid overdose to patients and family members. Any person can request these Naloxone devices regardless of whether they are taking opioid medications or not and usually do not require a prescription (i.e. you can walk up to any pharmacy and request it).

## TAKE THE FOLLOWING STEPS IF YOU SUSPECT AN OPIOID OVERDOSE

**STEP 1: CALL FOR HELP and DIAL 911. AN OPIOID OVERDOSE NEEDS IMMEDIATE MEDICAL ATTENTION.**

**STEP 2: CHECK FOR SIGNS OF OPIOID OVERDOSE**

Signs of OVERDOSE and/or OVERMEDICATION, which often results in death if not treated, include:

- 1) Mental confusion, slurred speech, intoxicated behavior
- 2) Nodding off during conversation or activity
- 3) Unusual or Extreme sleepiness, inability to awaken verbally or upon sternal rub
- 4) Breathing problems or respiratory distress
- 5) Slow to shallow breathing in a patient that cannot be awakened
- 6) Fingernails or lips turning blue/purple.
- 7) Small “pinpoint” pupils
- 8) Slow heartbeat and/or low blood pressure
- 9) Hearing the “death rattle”: an exhaled breath with a very distinct, labored sound coming from the throat

**STEP 3: SUPPORT THE PERSON’S BREATHING:** Start rescue breathing which can be very effective in supporting respiration. Start full CPR is needed.

(Rescue breathing for adults involves the following steps: Be sure the person’s airway is clear, check that nothing inside the person’s mouth or throat is blocking the airway. Place one hand on the person’s chin, tilt the head back and pinch the nose closed. Place your mouth over the person’s mouth to make a seal and give 2 slow breaths. The person’s chest should rise (but not the stomach). Follow up with one breath every 5 seconds.)

**STEP 4: ADMINISTER NALOXONE:** If available Naloxone injection is approved by the FDA and has been used for decades by EMS personnel to reverse opioid overdose and resuscitate individuals who have overdosed on opioids. Naloxone can be given intranasal with the NARCAN Nasal Spray or intramuscular (into the muscle) injection with EVZIO.

Once patient starts breathing independently, put them in the “recovery position” on the side and always stay with the patient and keep them warm. Do not put in cold bath due to risk of drowning and do not try to make the patient vomit the drugs due to risk of choking or aspiration.

The NARCAN Nasal Spray: is a pre-filled, needle-free device that requires no assembly. To use remove from package and deliver a single dose into one nostril. If needed you can Re-administer NARCAN Nasal Spray using a new NARCAN nasal spray in alternative nostrils 2 to 3 minutes

after first dose if the patient does not respond or responds and then relapses into respiratory depression.

The EVZIO Auto-Injector is injected into to the muscle. Remove from package. Pull EVZIO out of the outer case and remove safety guard. Once turned on, the device provides verbal instruction to the user describing how to deliver the medication, similar to automated defibrillators. Place black end against the middle of the patient's outer thigh, through clothing if necessary, then press firmly and hold for 5 seconds, Can inject a second dose of EVZIO 2to 3 minuted after first dose if if the patient does not respond or responds and then relapses into respiratory depression. EVZIO comes with a trainer device that all family members should practice with prior to a real emergency.

Both NARCAN Nasal Spray and EVZIO are packaged in a carton containing two doses, to allow for repeat dosing if needed. Always call 911 after administration of Naloxone products.

**NOTE: It is important to seek medical care or call 911 after the administration of Naloxone, even if the patient fully awakens, as the patient can become unconscious again once the Naloxone wears off.**

**NOTE: All naloxone products have an expiration date, so it is important to check the expiration date and obtain replacement naloxone as needed.**

SIDE EFFECTS: Note Naloxone products are contraindicated in patients with known allergies to naloxone hydrochloride or any other ingredient in naloxone. Use with caution in patients with cardiac disease or history of seizures. Note naloxone is category C in pregnancy. In each of these cases always call 911 and the benefit of saving a life may still outweigh the risk of death and adverse side effects.

Patients who are physically dependent on opioid therapy will experience opioid withdrawal with the administration of naloxone, in these individuals although unpleasant opioid withdrawal is not considered to be life threatening. In each of these cases always call 911 and the benefit of saving a life may still outweigh the risk of death and adverse side effects.

(If you do not have a Naloxone nasal spray or the EVZIO auto-injector device, please ask your provider or your pharmacist for one.)

**(MYPAINTOOLS)**

*(Picture: MyPainTools)*



The last point that I want to make is the most important point when it comes to the treatment of chronic pain and the use of opioid therapy. Self-management of pain is an important part of your treatment plan. Active self-management techniques must be included in your treatment plan. Active techniques in the form of mastered self-initiated skills such as pacing your activities, self-massage and self-relaxation therapy for example are important. These techniques when combined with treatments such as psychology, cognitive therapy, acupuncture and interventional injections can have both synergistic and medication-sparing effects. This will allow you to obtain the function and pain relief you desire while minimizing the amount of opioid medications needed to achieve those goals. As stated before it is important to have a well-rounded treatment plan that incorporates multiple different modalities to help control and manage your pain as this will allow a better quality of life and the need for fewer medications, such as opioids. You should think of your treatment plan like a “Bowl Of Soup” and think of the different treatments as ingredients in your soup. You want to use as many healthy “ingredients” such as acupuncture, exercise, biofeedback, etc. in addition to other treatments such as opioid therapy. Life style modifications are also one of these additional modalities that need to be considered. If you have time and wish to learn more please read the optional section on additional information about opioid therapy.

END OF COURSE NOW TAKE QUIZ

OPIOID SAFETY PROGRAM QUIZ

- 1) The self-administration of medications to alter one's state of consciousness ("get high") is known as:
- Use
  - Abuse
  - Cloud 9
  - Illicit Use

(CORRECT ANSWER IS "B": Abuse is the self-administration of medications to alter one's state of consciousness ("get high"). This is an intentional, maladaptive pattern of use of a medication (whether legitimately prescribed or not) leading to significant impairment or distress, such as repeated failure to fulfill role obligations, recurrent use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems, and usually occurring over a 12-month period.)(QUESTION FROM "TERMINOLOGY")

- 2) To get the best and fastest pain control your doctor should start you on higher rather than lower doses?
- TRUE
  - FALSE

(CORRECT ANSWER IS "FALSE": It is important to understand that the lowest dose need for effective pain control is recommended. Higher doses do not translate into better pain relief in many cases. )(QUESTION FROM "SAFETY")

- 3) Opioid therapy is a good option for all patients?
- TRUE
  - FALSE

(CORRECT ANSWER IS "FALSE": Opioid therapy is not right for everyone. Your doctor will determine after a taking a thorough physical and medical history to determine if the use of opioid therapy is an appropriate option to add to your treatment plan.)(QUESTION FROM "PATIENT ASSESSMENT")

- 4) The most important thing your pain medications provide you is a decrease in your pain score?
- a. TRUE
  - b. FALSE

(CORRECT ANSWER IS “FALSE”: As a patient it is more important to evaluate yourself for improvement in function than improvement in pain scores.)(QUESTION FROM “PAIN RELIEF VS FUNCTION/ADL”)

- 5) It is not necessary for you to obtain additional information for yourself about the medications you take and your medical condition, as your doctor will tell you everything you need to know?
- a. TRUE
  - b. FALSE

(CORRECT ANSWER IS “FALSE”: You should empower yourself through further education not only about your medical condition but also about your medications and the treatment options available to manage your condition.)(QUESTION FROM “ADJUVANT THERAPIES”)

- 6) Absolute contraindications to the use of opioid therapy includes:
- a. Significant Respiratory Depression
  - b. Acute or severe chronic bronchial asthma
  - c. Known or suspected paralytic ileus
  - d. Hypersensitivity to the medication
  - e. All of the above

(CORRECT ANSWER IS “E”: All of the above are absolute contraindications to the use of opioid therapy.)(QUESTION FROM “MEDICATION SIDE EFFECTS”)

- 7) Your physician may use all of the following to ensure your safety and appropriate use of opioid medications, EXCEPT:
- a. CURES
  - b. UDS
  - c. PILL COUNTS

- d. All of the above

(CORRECT ANSWER IS “D: All of the above are used to ensure your safety and appropriate use of opioid medications)(QUESTION FROM “ONGOING THERAPY AND MONITORING)

- 8) It is your responsibility to make sure your medications is safely stored and out of reach of others?
  - a. TRUE
  - b. FALSE

(CORRECT ANSWER IS “TRUE”: It is important and your responsibility to keep your opioid medication stored in a safe, secure, dry place, where a pet, child, teenager, family member, or stranger cannot get to them.)(QUESTION FROM “MEDICATION SAFE STORAGE AND DISPOSAL)

- 9) Which of the following is a reason to discontinue chronic opioid therapy for a patient who has been receiving opioids for management of a chronic pain conditions:
  - a. Medication side effects
  - b. Patients wish to stop their medications
  - c. Loss of benefit from medications
  - d. Misuse or abuse of medications
  - e. All of the above

(CORRECT ANSWER IS “E”: There are several reasons to discontinue chronic opioid therapy for a patient who has been receiving opioids for management of a chronic pain conditions. These include medication side effects, patients wish to discontinue opioid therapy, loss of meaningful clinical benefit from the medications, misuse or concerns regarding adherence to the treatment agreement and office policies, reduction in one’s pain no longer requiring opioid therapy, and as well as changes in one’s health resulting in opioid therapy being more harmful than beneficial.)(QUESTION FROM “DISCONTINUING OPIOID THERAPY”)

- 10) Having a glass of wine with dinner when one is taking chronic opioids is always safe?
  - a. TRUE
  - b. FALSE

(CORRECT ANSWER IS “FALSE”: Patients often wonder if a is small consumption of alcohol while on pain medications, such as a glass of wine with dinner is safe? This is a difficult



question to answer due to individual differences between patients, and it is impossible to know in advance how much is “too much” alcohol. Concerning symptoms that you should watch out for include drowsiness, confusion, or dizziness. If you experience these side effects seek medical care immediately. Again we strongly recommend you do not consume alcohol while taking opioid medications as well as if you are taking benzodiazepines. Benzodiazepines combined with alcohol with or without opioid medications have similar serious concerns for overdose and death and should be avoided.)(QUESTIONS FROM “CO-USE WITH BENZODIAZEPINES AND ALCOHOL”)

- 11) Driving after taking an opioid medication could result in a driving under the influence (DUI) or driving while intoxicated (DWI) charge if the police officer feels you are impaired, even if you have a legal prescription?
- TRUE
  - FALSE

(CORRECT ANSWER IS “TRUE”: California also has some particularly strict laws when it comes to “drugged driving,” according to the unofficial DMV Guide. The law does not distinguish between illegal drugs, opioid prescription drugs, alcohol and even over-the-counter remedies. Even driving after taking an over-the-counter medication, that causes drowsiness, could result in a driving under the influence (DUI) or driving while intoxicated (DWI) charge if the police officer feels you are impaired, even if you have a legal prescription. Always err on the side of safety and use caution with any medication, especially opioids when driving.)(QUESTION FROM “DRIVING AND OPIOIDS”)

- 12) The most important take home message from the Opioid Safety Program is:
- Opioids are bad and should never be used
  - If you misuse opioid medications you are “bad” person
  - Opioids are safe to use for everyone
  - Self-management of pain is an important part of your treatment plan

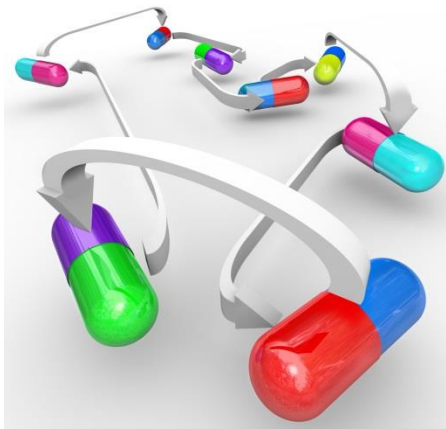
(CORRECT ANSWER IS “D”: All of above are false except choice “D”. Self-management of pain is an important part of your treatment plan. Active self-management techniques must be included in your treatment plan. Active techniques in the form of mastered self-initiated skills such as pacing your activities, self-massage and self-relaxation therapy for example are important. These techniques when combined with professional interventions can have both synergistic and medication-sparing effects. This will allow you to obtain the function and pain relief you desire while minimizing the amount of opioid medications needed to achieve those goals.)(QUESTION FROM “MYPAINTOOLS”)

END OF COURSE: THANK YOU FOR YOUR TIME

OPTIONAL SECTION: OPIOID SAFETY COURSE

**(OPIOID CLASSIFICATIONS)**

*(Picture: Opioid Classifications)*



Although the term opiate is often used as a synonym for opioid, the term opiate is properly limited to the natural alkaloids found in the resin of the opium poppy (*Papaver somniferum*).

The opium poppy was cultivated as early as 3400 BC in Mesopotamia. The term opium refers to a mixture of alkaloids from the poppy seed. Opiates are naturally occurring alkaloids such as morphine or codeine. Opioid is the term used broadly to describe all compounds that work at the opioid receptors. The term narcotic (from the Greek word for stupor) originally was used to describe medications for sleep, then was used to describe opioids, but now is a legal term for drugs that are abused as well.

OPIOID CLASSIFICATIONS			
NATURALLY OCCURING	Morphine	SYNTHETIC	Meperidine
	Codeine		Fentanyl

	Papavarine		Remifentanil
	Thebaine		Alfentanil
	Mitragyna Speciosa		Sufentanil
	Salvinorin A		Methadone
SEMISYNTHETIC	Diamorphine		Dextropropoxyphene
	Dihydrocodeine		Butorphanol
	Hydromorphone		Levorphanol
	Hydrocodone		Pentazocine
	Oxycodone	ENDOGENOUS	Endorphins
	Oxymorphone		Enkephalins
	Ethylmorphine		Dynorphins
	Buprenorphine		Endomorphins
	Diamorphine (Heroin)	UNIQUE DRUGS	Tramadol
	Nalbuphine		Tapentadol

Most opioid medications are in the oral formulation but some of the opioids do come in a patch option. The two most common used opioid patches currently include the fentanyl patch and the buprenorphine patch, also known as the Butrans® Patch. Extra caution should be taken with the use of the Fentanyl patch in the elderly and is contraindicated in the opioid-naïve patient (patients who are taking less than 60mg of morphine equivalence daily).

Fentanyl patches are advantageous in patients who are unable to swallow pills. The disadvantage with fentanyl patches is their delayed onset of action and being highly protein-bound they increase the risk of overdose in frail patients (decreased plasma protein resulting in higher free fentanyl levels combined with the reduced ability to metabolize fentanyl). As body temperature increases, the absorption of the drug can increase, and therefore may be problematic with febrile patients or those who use heating pads, etc. Once the patch is removed, the time to drug elimination is significantly longer (>24hours) in the elderly patient. These patches also have a higher risk of skin rashes which can be very uncomfortable for the patient who have sensitive skin.

An alternative to the Fentanyl patch is the Butrans® Patch, which contains the medication buprenorphine. These patches have the advantage of being better tolerated in elderly patients and a decrease risk of over sedation and other side effects. They also can be used in opioid naive patients. They are good options when strong opioids are undesirable. They also have lower abuse potential and milder withdrawal symptoms. In elderly patients, buprenorphine patches may have altered pharmacokinetics due to poor fat stores, muscle wasting or altered clearance; therefore they should be used with caution with skinny patients. Patients on high doses of morphine and/or strong opioids should NOT be switched to transdermal buprenorphine due to its

potential to precipitate opioid withdrawal. The Butrans® patch also has similar concerns of a skin rash and increased absorption of the drug with higher body temperature as does the fentanyl patch.

## (MECHANISM OF ACTION)

*(Picture: Mechanism of Action)*



Opioids can be a life changing medication for many patients with chronic pain, if used responsibly. Opioids have great potential to ease pain; however they have equal potential for deadly side effects and misuse as stated before.

Opioids mimic the actions of endogenous opioid peptides by interacting with mu, delta or kappa opioid receptors. Opioids work by binding to opioid receptors in the central and peripheral nervous system where they produce analgesic effects by decreasing the perception of pain, decreasing your reaction to pain, and increasing pain tolerance. They do not have an effect on the source of the pain, such as anti-inflammatory medications by reducing inflammation.

There are many types of nerve fibers in our body. The two main nerve fibers types that are involved in the perception of pain are known as C-fibers and A-delta fibers. When opioids bind to opioid receptors located on these nerve fibers they block the release of pain neurotransmitters (through a complicated process which we do not need to discuss here otherwise you would fall asleep reading it). The blocking of these neurotransmitters, such as glutamate, substance P, and calcitonin gene-related peptide from the nociceptive fibers, results in analgesia (i.e. pain relief).

Opioids also bind to other opioid receptors throughout the body, such as gastrointestinal tract, producing unwanted side effects such as constipation, respiratory depression, and sedation. They also often produce euphoria, which is one of the reasons their use can lead to abuse, misuse and addiction.

## (LONG ACTING VS SHORT ACTING OPIOIDS)

*(Picture: Long Acting vs Short Acting Opioids)*



There are three classifications of chronic pain: intermittent, persistent and breakthrough pain. There are also two different forms of pain medications: short acting and long acting opioid medications.

Persistent or constant pain is characterized by pain that lasts for 12 or more hours every day. The pain is usually treated with medicines that last around the clock, such as long acting opioids, adjuvant medications and with non-drug therapies. This form of pain is common with chronic pain. For patients with chronic pain, the classic approach is to convert the patient from short-acting opioids to long-acting/sustained release opioids, because long-acting opioids provide less fluctuation in analgesic blood levels, fewer adverse effects, and require less frequent dosing.

Intermittent pain is characterized as episodic and may occur in waves or patterns. Intermittent pain is typically treated with non-drug therapies and a short course of adjuvant medications such as NSAIDs, however intermittent moderate to severe pain may be treated with short-acting opioids. Intermittent pain is usually not persistent. It is possible to have both persistent pains, such as chronic low back pain, in addition to intermittent pain, such as acute migraines.

Breakthrough or sudden pain is characterized by a flare-up or a break through the relief provided by an around the clock pain medicine regime used to treat persistent pain. Non-drug therapies, adjuvant medications and occasionally short-acting opioid medications can be used to treat breakthrough pain. The CDC recommends that when starting opioid therapy for chronic pain, clinicians should first start by prescribing immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

Historically when using a combination of long acting and short acting medications many physicians recommend only one type of long acting opioid medication and one type short acting medication be used. Some recent studies have challenged this idea and have shown that lower doses of two different types of long acting or short acting medications may decrease the risk of tolerance and medication side effects compared to high doses of one type of medication. This is however a controversial topic. Each individual and their pain are unique and your pain specialist will determine the best treatment plan for you.

Whichever medications your doctor chooses, they will start you on the lowest doses and slowly titrate these medications till the needed effect is reached. Keep in mind that it is very important to take advantage of the opportunity that pain relief brings to make your life better. For most people, this means resuming activities that were stopped by the pain or illness. When opioids are used to eliminate pain without improving lifestyle or function, the medicine becomes the focus of your life and this can do more harm than good.

## **(REMS PROGRAM)**

*(Picture: REMS Program)*



State and federal departments are working together to also develop increased education and training for patients taking opioid medications to improve safety and reduce the risk of abuse, one of those programs which you may be required to comply with is known as the REMS program.

Effective March 25, 2008, the Food and Drug Administration Amendments Act of 2007 (FDAAA) reserved the right for the U.S. Food and Drug Administration (FDA) to order Risk Evaluation & Mitigation Strategies (REMS) for drugs or biologics with significant toxicity levels and/or demonstrable risk factors.

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks.

The FDA has required a REMS for extended-release and long-acting (ER/LA) opioid analgesics.

Under the conditions specified in the REMS, patients who take analgesics are strongly encouraged to do all of the following:

- 1) Be educated on the safe use, serious risk, storage and disposal of opioid medication, which this course has covered.
- 2) Obtain more specific information about the particular opioid medications you take by clicking on [Patient Counseling Document \(PCD\)](#).
- 3) Once on the PCD website click on **Medication Guides** and read the medication guide for the opioid medications you are taking. You should always be reading the Medication Guide that you will receive from your pharmacist every time an ER/LA opioid is dispensed to you, if you have not done so in the past.

#### Patient Counseling Document on Extended Release / Long-Acting Opioid Analgesics

The DOs and DON'Ts of

Extended-Release / Long - Acting Opioid Analgesics

#### DO:

- Read the Medication Guide
- Take your medicine exactly as prescribed
- Do store your medications safely and securely and keep them out of the reach of children, pets, and household members, to avoid risks from unintended exposure

- Flush unused medicine down the toilet after grinding with coffee beans (note you should check your city/state regulations and read the section on disposal of medications in this course before flushing any medications)
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

#### DON'T:

- Do not give your medicine to others
- Do not take medicine unless it was prescribed for you
- Do not stop taking your medicine without talking to your healthcare provider
- Do not break, chew, crush, dissolve, or inject your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider who will refer to the product labeling to determine if it is appropriate to sprinkle the contents of a capsule on applesauce or administer via a feeding tube
- Do not drink alcohol while taking this medicine
- Do not share these medications, even if someone has the same symptoms as you.

#### Call 911 Or Your Local Emergency Service Right Away If:

- You take too much medicine
- You have trouble breathing, or shortness of breath
- A child has taken this medicine

#### Tell Your Healthcare Provider:

- Your complete medical and family history, including any history of substance abuse or mental illness
- The cause, severity, and nature of your pain
- If the dose you are taking does not control your pain
- About any side effects you may be having



- About all the medicines you take, including over-the-counter medicines, vitamins, and dietary supplements
- Your treatment goals

Another part of the REMS programs deals with guidelines and recommendations that your physician may refer to when prescribing opioid medications, and this document is known as the: [FDA BLUEPRINTS](#).

### (SPECIAL CONSIDERATIONS)

*(Picture: Special Considerations)*



By now you have realized that this tutorial often repeats multiple times a similar point in different ways. This is not because we love to ramble on, but this is intentional as these points are the key points to this tutorial. Some research has shown that it takes multiple exposures to information before they become engraved into your brain. Some experts say it takes 16-21 times to make something a habit!

Use opioid medications for acute or chronic pain only after determining that alternative therapies do not deliver adequate pain relief. The lowest effective dose of opioids should be used.

When starting you on opioid therapy your physician will account for your opioid history, physical tolerance, and consideration of agents in mixed preparations, cross-tolerance, and

conversion irregularities. It is always best to use caution when initiating and increasing opioid regimens.

There have been many debates as to the safe range with regards to opioid therapies. When talking about opioid medications many often refer to what is known as morphine equivalent dose (MED).

Maximum safe dose is patient-specific and dependent on current and previous opioid exposure, as well as on whether the patient is using such medications chronically. Your doctor will slowly titrate up your dose until adequate pain relief is seen or side effects preclude further escalation.

The current guidelines do recommend consultation with a pain specialist if you are taking above a certain amount of opioid medications. If a patient’s dosage has increased over 120 mg MED per day, without substantial improvement in function and pain, they should consider seeking a consultation from a pain specialist. High dose opioid therapy has not been shown to be superior to lower dose treatment plans. Some studies have shown that risks of adverse events increase at doses at or above 120mg MED, therefore you should always try to decrease your overall dose of opioids as you medical condition improves or when possible.

<b>RECOMMENDED DOSE THRESHOLD FOR PAIN CONSULTATION</b>	
Codeine	800mg/24hours
Fentanyl Patch	50mcg/hour
Hydrocodone	120mg/24hours
Hydromorphone	30mg/24hours
Methadone	40mg/24hours
Morphine	120mg/24hours
Oxycodone	80mg/24hours
Oxymorphone	40mg/24hours

<b>OPIOID SPECIFIC PRECAUTIONS</b>	
<b>BUPRENORPHINE</b>	QTc Prolongation (Risk of Torsade de Pointe)
	Hepatotoxicity
	Application site skin reactions
	Increased drug exposure with increased core body temperature or fever
<b>METHADONE</b>	QTc Prolongation (Risk of Torsade de Pointe)
	Delayed Respiratory Depression
	Increased Clearance During Pregnancy
<b>FENTANYL PATCH</b>	Not for opioid naive people

	Application site skin reactions
	Increased drug exposure with increased core body temperature or fever
EXALGO®	Exalgo® contains sodium metabisulfite, an ingredient that may cause adverse reactions in people with allergies to sulfites. It's important to note that an allergy to sulfites is different from an allergy to sulfa drugs.
NUCYNTA®	Risk of Serotonin Syndrome
	Angioedema

Current opioids such as methadone should only be prescribed only by a pain medicine specialist or a physician thoroughly trained on the use of methadone. Safety concerns with methadone are due to its sometimes unpredictable pharmacodynamics and pharmacokinetics. Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone doses should not be increased more frequently than every 7 days. Never take more than prescribed when it comes to Methadone, as it can seriously lead to overdose and death.

Inform your doctor if you have or develop COPD, CHF, sleep apnea, alcohol or substance abuse, are over 65 years of age, or have history of or develop renal or hepatic dysfunction. These conditions may potentiate opioid adverse effects and require close monitoring. Even low doses of opioids can lead to more risks than benefits in some.

One of the major concerns with ongoing opioid therapy includes the risk of tolerance as explained in the terminology section. One tool your physician may use to deal with tolerance is known as opioid holiday or opioid rotation.

Opioid holiday usually is initiated when you are slowly titrated off your opioid medications with the help of your physician, and then allow a certain amount of time in which you are not exposed to opioid medications. This may allow your body to “reset its opioid receptors”, thus when opioid medications are restarted they become effective at lower doses and thus reduce side effects while increasing efficacy.

Opioid rotation is defined as a change in opioid drug or route of administration with the goal of improving outcomes. Switching from one opioid to another is often necessary to realize the most favorable balance of therapeutic effects and side effects in patients who require chronic opioid analgesic therapy as a component of overall pain management.

Your physician will use what is known as an opioid conversion table when switching you to another pain medication. This conversion table will help your physician select a safe starting dose for the new opioid medication. It is always best to start low and error on the side of safety

and slowly titrate up if needed, rather than start high and risk overdose. Due to opioid cross tolerance opioid cross-tolerance experts actually recommend that a dose reduction of up to 50% is appropriate and safe when switching from one opioid to an alternative.

(SUBOXONE®)

It is important to discuss a medication that is often used to treat addiction in individuals who have chronic pain but also have opioid dependence or additional concerns. This medication is known as Suboxone®.

Suboxone® contains a combination of buprenorphine and naloxone. This should not be confused with Subutex® which is an opioid medication that only contains buprenorphine. Buprenorphine is an opioid medication, thus Suboxone® is an opioid medication as well. It has less risk of addiction due to the addition of naloxone and the fact that buprenorphine is a part-agonist and binds strongly to the opioid receptor often blocking the effects of other opioid medications.

The basic issue with analgesia in the buprenorphine-maintained patient is that while buprenorphine has analgesic properties, it is a partial agonist. This means that not only will it block the cravings associated with opioid dependence, but because of the high affinity of buprenorphine for opioid receptors it may also block the analgesic effect of OTHER opioids. However since buprenorphine itself binds strongly to the opioid receptor it provides analgesia and is often used to treat moderate to severe chronic pain.

You physician may recommend you see a pain medicine specialist trained and licensed to use Suboxone® if they are concerned with you developing opioid dependency and/or opioid addiction.

Suboxone's® labeled use and indication is for opioid dependence. However since it contains buprenorphine it does provide analgesia in patients with chronic pain. Suboxone® can only be written by specially trained and licensed physicians. If you are on Suboxone® you should read fully the medication guide that you received from the pharmacy when you obtained your medication.

The labeled uses of Buprenorphine include both management of moderate to severe chronic pain only in the patch form (i.e. Butrans®) and the treatment of opioid dependency, Suboxone®.

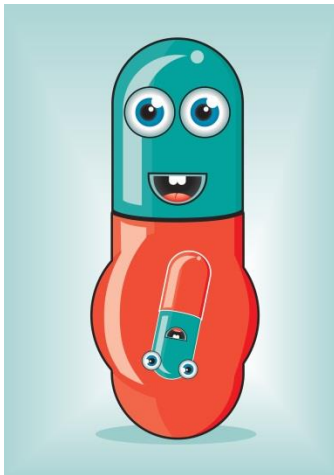
Of note the Butrans® patch is a patch that contains the medications buprenorphine, however the concentration of buprenorphine in the Butrans® patch is significantly less than that in Suboxone® and Subutex®, thus the Butrans® patch is a good option for patient with moderate to severe chronic pain who need around the clock opioid medications. And due to the low

concentrations of buprenorphine in the Butrans® patch, most patients can still take other breakthrough pain medications, such as Vicodin® or Percocet® while on the Butrans® patch and still obtain significant pain relief from their breakthrough medications.

Methadone is another drug that has a labeled indication for both moderate to severe pain as well as for the detoxification and maintenance treatment of opioid addiction through a certified program. Buprenorphine is considered to be less addictive than methadone. Use of methadone for other purposes than the treatment of pain, such as addiction, requires special training and a special license, and usually only allowed through certified programs.

## **(OPIOIDS AND PREGNANCY & BREASTFEEDING)**

*(Picture: Opioids and Pregnancy & Breastfeeding)*



### **(PREGNANCY)**

If you are pregnant or planning to get pregnant you should talk to your physician with regards to the safety of opioid therapy during your pregnancy. These guidelines also include reproductive-aged women who are not planning a pregnancy but might be at risk of an unintended pregnancy.

If you have been taking an opioid for a long time you should not just stop suddenly. This could cause you to go into withdrawal which could be harmful to you and may cause harm to your

pregnancy. Talk with your health care provider about the risks and benefits of continuing or stopping your medication. Any reduction in your medication needs to be done very gradually, and carefully monitored by your health care provider.

There is inadequate data on human pregnancy exposure to opioids to rule out teratogenic risks completely, although the limited data available do not indicate substantial teratogenic effects. Indiscriminate use should be avoided.

According to the Centers for Disease Control and Prevention (CDC) the effects of opioids on a pregnant woman and her unborn baby are not well understood. Previous research has shown that opioid analgesic use and abuse have been increasing in recent years but their effects on the developing fetus are poorly understood.

According to an ongoing, population-based study conducted by the CDC, women receiving opioid analgesic treatment in early pregnancy had a 2- to 3-fold increased risk of delivering infants with ventricular septal defects, atrioventricular septal defects; hypoplastic left heart syndrome, spina bifida, or gastroschisis. Although the absolute risk for any individual woman is relatively modest, caution should be used while pregnant.

Some studies have suggested that opioid exposure in the first trimester may be associated with heart defects and other birth defects. Based on these studies the risk appears to be small. Several other studies have not supported an increased risk for heart defects or birth defects in general. Opioids are not known to decrease the likelihood of you becoming pregnant.

At this time the only Category B opioid is oxycodone. You should avoid benzodiazepine use at all times during pregnancy due to its risk on the development of the fetus. Other fetal adverse events with the use of opioid therapy during pregnancy include miscarriage, premature birth, fetal growth restriction, low birth weight, and birth defects such as heart defects and spina bifida.

You and your physician must weigh the benefits of these medications along with their potential risks when discussing analgesic treatment options with you, if you are or may become pregnant. Uncontrolled pain during pregnancy itself can endanger the mother as well as the fetus due to for example severe hypertension among other things.

One of the biggest concerns with the use of opioids during pregnancy is the development of neonatal withdrawal syndrome in the baby after delivery. This is due to the fact that the fetus is exposed to opioids through the placenta during pregnancy and after delivery the baby is no longer exposed to the medication. If you are taking opioid therapy your OB/GYN doctor will discuss the possibility of your baby needing to stay a few nights in the NICU for close monitoring. The degree of fetus exposure to opioid medications will often determine the intensity of the withdrawal severity post-delivery. Always inform your doctor if you are taking any amounts of opioids during pregnancy. It is best that you inform all of your doctors of all your medications when pregnant.

The length of time and the amount of medication you have been taking can influence the likelihood of withdrawal in the newborn. Withdrawal usually begins within the first 24 hours after birth, but can occur up to 2-3 weeks later. It is important that you are aware of the signs of withdrawal which include: irritability, sneezing, runny nose, tremors, vomiting, difficulty breathing, extreme drowsiness, poor feeding, sweating, diarrhea and occasionally seizures. Cases of untreated withdrawal can lead to seizures and death.

With proper treatment most babies can be supported through the withdrawal process. Withdrawal in the newborn does not appear to be associated with any long-term complications.

There is no information to suggest that opioids taken by the father would adversely affect a pregnancy, however there may be an effect on a male's sperm count and sexual function due to testosterone lowering effects of opioids.

#### (BREASTFEEDING)

Breastfeeding during opioid therapy is also an important topic to discuss with your physician. Many consider breast milk to be the best food for their baby, and some argue that if one stops breastfeeding they risk losing their milk supply. Always check with your baby's pediatrician with regards to the safety of breastfeeding while on opioid therapy as individual considerations need to be addressed.

Always use the lowest dose of opioids needed to treat your pain. Consult your pharmacist or physician with regards to additional recommendations.

All opioids are known to be found in breast milk, mostly in very small amounts. If you need to take an opioid while breastfeeding you should take as low a dose as possible and for as brief a period of time as necessary.

If at all possible, breastfeeding should be timed to avoid the peak amount of the drug in your system. An alternative to breastfeeding is the use of formula, which is a personal choice. If you pump, you may want to consider pumping in the morning and taking your medications after you pump and avoiding night time doses. Opioid medications are at their highest concentration in the body during the first 1 to 2 hours after taking them. You should consider avoiding breastfeeding during this time.

Breastfed infants whose mothers are taking an opioid should ALWAYS be very carefully and watch for any signs of drowsiness. Concerning signs to watch for include: the baby being sleepier than normal, breastfeeding pattern changes, you notice constipation in your baby, baby becomes difficult to arouse for feeding, and the baby's ability or effort to suck effectively decreases. If any of these side effects are noticed, either the opioid or the breastfeeding should be stopped and the child should be seen by a pediatrician immediately and if necessary call 911.

All opioids are category C, except for Oxycodone which is category B.

In animal studies on pregnancy and oxycodone, the medication did not seem to increase the risk of birth defects or other problems. However, as a narcotic, oxycodone can cause withdrawal symptoms in the infant after delivery.

Please note that Oxycontin® which is a long acting form of Oxycodone is category C. Please also note that oxycodone often is in combination for example with other medications such as NSAIDs are not recommended during pregnancy. Please note alcohol and/or benzodiazepine use are absolutely contraindicated during pregnancy.

United States FDA Pharmaceutical Pregnancy Categories	
<b>Pregnancy Category A</b>	Adequate and well-controlled human studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
<b>Pregnancy Category B</b>	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.
<b>Pregnancy Category C</b>	Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
<b>Pregnancy Category D</b>	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
<b>Pregnancy Category X</b>	Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

**(OPIOIDS AND THE ELDERLY)**



*(Picture: Opioids and the Elderly)*



Pain treatment in the elderly is an important challenge in today's time due to increasing numbers of senior citizens, their higher incidence of pain, and their greater susceptibility to adverse effects of pain medication in this population. Opioids as a class may be less likely to cause organ toxicity than NSAIDs (i.e. GI bleeds) in senior citizens. According to these guidelines, opioid therapy for elderly patients may be safe over the long term, but can be dangerous when starting or increasing a dose.

When it comes to risks of opioid use in the elderly the primary concerns are constipation, overdose, over sedation and falls. To minimize these effects the following precautions are recommended in elderly patients: lower starting doses, slower titration, longer dosing intervals, more frequent monitoring, and discontinuing (by tapering) benzodiazepine use when possible.

Practical recommendations for opioid prescription in the elderly include meticulous review of indication for opioid use, not only initially but also at regular intervals thereafter. A policy of careful titration should be followed, with conservative choice of dosage on starting. Dosing intervals may need to be lengthened subsequently. It is very important in assessing concurrent or undisclosed use of medications, such as over-the-counter NSAIDs, other opioids, and benzodiazepines or other sedatives (including alcohol), that place patients at higher risk for morbidity or mortality. Assessment of the patient's ability to reliably self-administer should also be considered, especially if signs of cognitive impairment are apparent and he or she is still living independently.

As with all patients, including senior citizens it is important that you disclose all your prescription and over-the-counter medications (including alternative medications) and any alcohol consumption to your doctor.

Before prescribing an opioid, an environmental assessment for potential addiction/diversion risk should be conducted. The elderly may be a target for drug theft, etc. Proper storage and limited discussion surrounding the opioid is prudent.

Of all the unwanted effects of the opioids in the elderly, the most difficult to deal with is that of constipation, and severe cases can lead to deadly bowel injury. Incorporate an appropriate bowel

regimen, as this is essential in preventing constipation. Laxatives may be necessary. Polyethylene glycol and lactulose have more evidence for efficacy; however, other choices such as senna or bisacodyl might be considered on the basis of an individual patient's symptoms, toleration, and preferences.

Risk of delirium from opioids, since opioids are predominantly renally excreted, increases as creatine clearance (CrCl) worsens. This can happen with acute causes of reduced renal function (e.g., dehydration or drug interactions such as with NSAIDs and angiotensin-converting enzyme inhibitors). Other causes of delirium, such as patients taking their medications incorrectly, should also be explored.

One of the reasons why elderly patients are increasingly vulnerable to adverse drug effects and interactions is due to the higher rates of polypharmacy (i.e. taking a large number of different medications) and comorbidities.

Aging affects opioid pharmacokinetics via altered body composition (distribution volumes) and organ function (liver = metabolism, kidney = excretion). Pharmacodynamics is affected via impaired neurotransmitter/peptide production and changed receptor affinities/populations. The net effects of changes in opioid pharmacology with age on clinical opioid analgesia remain unclear, probably due to the significantly greater variability in body function with increasing age.

Pharmacokinetic factors that put the elderly at higher risk for opioid overdose than younger patients also includes lower serum binding, lower stroke volume (which acts to slow liver metabolism), as well as a greater sensitivity to the psychoactive and respiratory effects of opioids.

It is important to monitor renal and liver function in elderly patients on a routine basis. Renal or hepatic impairments can lead to toxicity as most opioids are metabolized in the liver and excreted through the renal system.

Methadone, propoxyphene, and meperidine are not recommended for use in elderly people and in patients with renal disease, because of the toxicity of their metabolites

Due to the fact that tolerance to the respiratory depressant effects of opioids develops slowly elderly patients with Pneumonia, COPD and/or sleep apnea are at greater risk for respiratory depression. Inform your doctor if you develop a lung disease such as Pneumonia as you may need to consider lowering your doses until the pneumonia resolves. Opioids may be a risk factor for central sleep apnea in the elderly. Elderly patients on opioid therapy also have high sleep disorders, as this may be a reflection of the effects of pain, or the sedating effects of opioids and/or concurrent depression. Last but not least elderly patients on opioid therapy are at risk of cognitive impairment. Patients with a psychiatric diagnosis or patients who live alone on opioid therapy should arrange some type of medication supervision to improve safety.

Elderly patients and their caregivers should be educated to recognize signs of overdose (i.e. slurred or drawling speech, emotional instability, mood changes, incoordination, nodding off during conversation or activity) so that the appropriate steps can be taken to minimize further harm.

Some recommended guidelines for elderly patients considering opioid therapy include starting initial doses at lower than the suggested initial adult dose and lengthening the time interval between dose increases. Always use weaker opioids and the lowest dose when possible, such as codeine, tramadol, hydrocodone or the Butrans patch. Among strong opioids, oxycodone and hydromorphone may be preferred over oral morphine for the elderly if constipation and sedation are an issue. Morphine should also be used with caution in patients with decreased renal function as the M-6 glucuronide metabolite of morphine accumulates and has been associated with severe adverse effects.

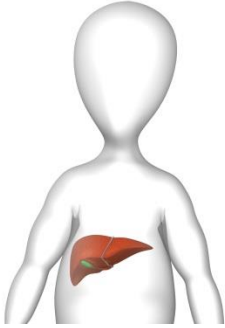
The combination of opioids and benzodiazepines increases the risk of sedation, overdose, falls and diminished function in all patients, especially as age advances.

For elderly patients who cannot tolerate pills your doctor may consider patches or solutions. Morphine solutions are useful in some situations such as patients with swallowing problems, or patients requiring less than 5 mg morphine per tablet. The two most commonly used opioid patches currently include the fentanyl patch and the buprenorphine patch, also known as the Butrans Patch.

Finally, it should be remembered that untreated pain in the elderly may have further adverse effects on the health of the patient. Persistent pain and its inadequate treatment is associated with a number of adverse outcomes in the elderly including functional impairment, falls, slow rehabilitation, muscle deconditioning, mood changes, decreased socialization, poor sleep and appetite disturbance, and greater health care use and costs.

## **(PATIENT WITH LIVER AND RENAL DYSFUNCTION)**

*(Picture: Patients with Liver and Renal Dysfunction)*



A very important topic with regards to opioid therapy is the special considerations that must be taken into account in patients who develop liver and renal (i.e. kidney) dysfunction. Although chronic opioid therapy has minimal long-term effects on organs, organ dysfunction can have a dramatic effect on side effects from these medications.

As in any clinical setting, the ‘right dose’ of an opioid analgesic medication is that which provides adequate pain relief in conjunction with an acceptable side effect profile.

It is important to monitor renal and liver function in patients taking chronic opioids and before starting opioid therapy. Renal or hepatic impairments can lead to toxicity as most opioids are metabolized in the liver and excreted through the renal system. We recommend that you get annual liver and renal function tests from your primary care doctor and inform all your physicians if there are any abnormal results.

#### (HEPATIC)

In hepatic failure, opioid clearance is reduced and drug bioavailability is increased. These changes can be secondary to reduced hepatic blood flow (limiting first-pass metabolism) and/or decreased CYP450 enzyme levels in these patients. It is recommended that if used, opioid dosing should be reduced to 50% of the recommended starting doses in these patients.

Morphine, oxycodone, hydromorphone and tramadol can usually be used cautiously in hepatic failure by means of downward adjustment of the dose and/or upward adjustment of the interval between doses.

Methadone, codeine and meperidine should be avoided in patients with liver failure. Codeine is a prodrug that is hepatically converted to morphine by the liver. In patients with liver dysfunction, pain control can be compromised if codeine is not metabolized. Meperidine is metabolized by liver to normeperidine. In hepatic disease, meperidine clearance is reduced and its half-life is prolonged. Seizures, a major side effect of meperidine and normeperidine, can occur at reduced doses in patients with hepatic failure. Methadone should not be used in the presence of significant hepatic failure unless absolutely no alternative exists. This is simply because the risk of excessive blood levels of methadone developing will be greater, and more unpredictable.

Combination drugs that include opioid medications (such as oxycodone and hydrocodone) with acetaminophen and NSAIDs (i.e. Norco®, Vicodin®, Percocet®) are limited by the non-opioid component, and overconsumption of acetaminophen containing products is hepatotoxic, and overconsumption of NSAID containing products can be toxic to the kidneys.

Fentanyl's pharmacokinetics are considered to be unchanged by liver failure, however its half-life is prolonged in liver failure with repeated dosing or high dose therapy. Transdermal fentanyl has not been adequately studied in liver failure. Hepatic failure can alter skin permeability and drug absorption; the clinical relevance of this, if any, has not been determined. Some experts suggest fentanyl is a preferred opioid in liver failure as it is for patients with renal failure as well, although this judgment appears to be entirely empiric.

Buprenorphine is metabolized in the liver, and its metabolites are excreted into the bile. (They are also, to a lesser extent, excreted by the kidneys.) There are some reports of acute liver toxicity associated with buprenorphine in the presence of liver disease, but information about its use in this situation is otherwise quite sparse.

The liver plays an important role in the presystemic clearance of orally administered oxymorphone, thus should be used with caution or avoided in liver dysfunction.

#### (RENAL)

The absorption, metabolism, and renal clearance of opioids are complex in renal failure. However, with the appropriate selection and titration of opioids, patients with renal failure can achieve analgesia with minimal risk of adverse effects.

Codeine and meperidine are not recommended for use in people with renal disease, because of the toxicity of their metabolites. Also not recommended is propoxyphene which has been taken off the USA market due to cardiac toxicity. There is debate as to the safety of morphine in patients with renal dysfunction due to buildup of active and toxic metabolites. If used, as with all opioids, we recommend close monitoring for sedation and other signs of toxicity.

Safer choices for patient with renal disease, but that still should be used with caution include hydromorphone, oxycodone, oxymorphone and hydrocodone.

The safest opioids to consider in patients with renal dysfunction include fentanyl and methadone. Fentanyl is considered relatively safe in renal failure as it has no active metabolites. Methadone is considered relatively safe in renal failure. It has no active metabolites and limited plasma accumulation in renal failure due to enhanced elimination in the feces. However, precautions regarding the use of methadone exist. It does not appear to be removed by dialysis.

Buprenorphine mainly undergoes hepatic elimination; there is minimal risk of accumulation in patients with renal impairment. Buprenorphine can be administered at normal doses in patients with renal dysfunction because it is mainly excreted through the liver. Buprenorphine are

unchanged in hemodialysis patients, which means that there is no need for dose-reduction with this drug. Thus, in patients with reduced renal function, chronic renal insufficiency and hemodialysis, buprenorphine appears to be a safe choice when opioid treatment is initiated.

Tramadol should be used with caution or avoided in patients with renal disease as tramadol's active metabolite is excreted renally and can accumulate with renal dysfunction.

The following guidelines have been proposed for the initial dosing of the safer opioids in renal failure.

- Creatinine Clearance > 50 mL/min: normal dosing.
- Creatinine Clearance of 10-50 mL/min: 75% of normal.
- Creatinine Clearance < 10 mL/min: 50% of normal.

In summary for most patients with renal or hepatic dysfunction always start at the lowest dose possible and caution should always be followed while monitoring closely for side effects.

<b>USE OF OPIOIDS IN PATIENTS WITH LIVER DYSFUNCTION</b>		
<b>APPEARS SAFE TO USE</b>	<b>USE WITH CAUTION (50% REDUCTION)</b>	<b>NOT RECOMMENDED TO USE</b>
Fentanyl	Morphine	Methadone
	Oxycodone	Codeine
	Hydromorphone	Meperidine
	Tramadol	Acetaminophen Products
	Oxymorphone	Vicodin®/Norco®
		Percocet®
		Buprenorphine
		Oxymorphone
<b>USE OF OPIOIDS IN PATIENTS WITH RENAL DYSFUNCTION</b>		
<b>APPEARS SAFE TO USE</b>	<b>USE WITH CAUTION (50% REDUCTION)</b>	<b>NOT RECOMMENDED TO USE</b>
Fentanyl	Morphine (mild dysfunction)	Morphine (moderate/severe)
Methadone	Hydromorphone	Codeine
Buprenorphine	Oxycodone	Meperidine
	Hydrocodone	Propoxyphene
	Oxymorphone	Tramadol
	Tramadol	

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the advice of a health-care professional. Any medical condition should be brought to the attention of, and discussed with, a qualified medical professional. It is your responsibility to seek emergency care or call your doctor if you have any concerns about your medical condition.

We understand that living with chronic pain may cause feelings of anger, helplessness or depression. You understand and agree that if you are experiencing these feelings, you must contact a counselor, social worker, psychologist or psychiatrist for help. If you are considering hurting yourself or have thoughts of suicide, you must immediately call 911 and seek medical care.

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