

Continuing Education

Pain Management and Opioid Dependence

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EDUCATIONAL OBJECTIVES:

1. Describe the experience of pain.
2. Differentiate between tolerance, dependence, addiction, and misuse and how they relate to opioids.
3. Describe the pharmacist's role in pain management.
4. Recognize the opioids used for addiction management.
5. List the limitations of using naloxone for outpatient distribution.

INTRODUCTION

Pain is an unpleasant, subjective, conscious, sensory and emotional experience that results from brain activity in response to a stimulus which engages the sensory, emotional, and cognitive processes of the brain.^{2,3} Pain, especially chronic pain, has multiple mechanisms that result in pain amplification and maintenance, including central and peripheral sensitization and altered modulation of pain perception.³ The assessment of pain requires a comprehensive examination of signs and symptoms as well as suspected pain mechanisms.³ Multiple measures exist for the assessment of pain symptoms, pain-related disability, psychological impact of pain, and candidacy for opioid management.³ Patients who present with pain as a chief complaint may be motivated to seek help due to fear, anxiety, disrupted sleep, functional and occupational disability, dependency, addiction, or other factors.³ Ultimately, these factors can influence patients' reported pain severity.³

CLASSIFICATION OF PAIN

Classifying pain is helpful to guide assessment and treatment. There are many ways to classify pain, and classifications may overlap. Pain can be classified based on the following characteristics:²

- Pain physiology (nociceptive, neuropathic, inflammatory)
- Intensity (mild-moderate-severe; 0-10 numeric pain rating scale)

- Time course (acute, chronic)
- Type of tissue involved (skin, muscles, viscera, joints, tendons, bones)
- Syndromes (cancer, fibromyalgia, migraine, others)
- Special considerations (psychological state, age, gender, culture)

Pain physiology can include nociceptive, neuropathic, and inflammatory pain.

Nociceptive pain represents the normal response to noxious insult or injury of tissues such as skin, muscles, visceral organs, joints, tendons, or bones. Neuropathic pain is initiated by a primary lesion or disease in the somatosensory nervous system. Sensory abnormalities can be perceived as numbness, hypersensitivity, and paresthesia.

Inflammatory pain results from the activation and sensitization of the nociceptive pain pathway by a variety of mediators released at a site of tissue inflammation. The mediators that have been implicated as key players are proinflammatory cytokines such as IL-1-alpha, IL-1-beta, IL-6 and TNF-alpha, chemokines, reactive oxygen species, vasoactive amines, lipids, ATP, acid, and other factors released by infiltrating leukocytes, vascular endothelial cells, or tissue resident mast cells.²

Pain intensity can be broadly categorized as mild, moderate, or severe. The use of a numeric scale is common in the healthcare field to rate pain intensity, where zero means no pain, and ten is the worst pain imaginable:²

- Mild: $\leq 4/10$
- Moderate: 5/10 to 6/10
- Severe: $\geq 7/10$

Acute pain is typically defined as less than three to six months duration. Chronic pain is typically defined as lasting more than three to six months, or persisting beyond the course of an acute disease, or after tissue healing is complete. Additionally, another time course

term is known as acute-on-chronic pain, which describes an acute pain flare superimposed on underlying chronic pain.²

Acutely, the major goals are pain control and relief while efforts are made to identify and treat the underlying disease and to enhance healing and recovery. Adequate management of acute pain may also prevent the development of chronic pain. Analgesics are the mainstay of acute pain treatment; however, nondrug methods such as patient education, heat/cold, massage, and distraction/relaxation are also essential. In some situations, regional analgesia and anesthesia are also indicated.²

In most cases of chronic pain, multiple mechanisms are at play, and the cause of the pain may be difficult to identify and eliminate. Pain relief is still the primary goal; however, improvement in function and quality of life are also of great importance.²

Pain relief can be attained through the use of analgesics such as opioids. Opioids play a unique role in society. They are widely feared compounds due to their association with abuse and addiction. Nevertheless, they are essential medications as they are some of the most effective drugs for the relief of pain and suffering. Historically, concerns about addiction have contributed to the undertreatment of disorders widely considered to be appropriate for opioid therapy, including cancer pain, end-of-life pain, and acute pain; however, their use for chronic non-malignant pain remains controversial.⁵

HISTORY

Opioid dependence is not a new problem. In fact, the ancient Sumerians cultivated poppies and isolated opium at the end of the third millennium B.C. Opium is believed to have been first used by priests to heal the sick and it was given with hemlock to allow people to meet death in a quick and painless manner.

Opium trading started with India and China and made its way across Asia to Europe by the thirteenth century. By the sixteenth century, opium drug abuse was already a well-documented problem and many countries made failed attempts to control the spread and use of opium. In 1806 the active ingredient morphine was isolated from opium and was being used in surgical procedures and general anesthesia. Unfortunately, morphine was found to be just as addictive and not any safer than opium. In 1898, heroin was synthesized and proclaimed to be a safer, more efficacious, and more potent version of morphine, but this has yet to be proven. Throughout the 1900s, more opiates were synthesized with the hope of finding a safer, yet efficacious alternative. Numerous opioids are on the market today and while some are considered a better alternative to morphine and heroin, they are all still addictive and contributing to the opioid epidemic today.⁶

OVERVIEW OF OPIOIDS

The term opioid describes all compounds that work at opioid receptors. Simply put, they are medications that relieve pain.¹ Specifically, the term opiate describes the naturally occurring opioids such as morphine and codeine.⁷ Opioids produce their effects by binding to opioid receptors: μ (mu), δ (delta), and κ (kappa). Opioids reduce the intensity of pain signals reaching the brain and affect those brain areas controlling emotion, which diminishes the effects of a painful stimulus.¹ Opioids differ from each other based on which receptors they bind and to what affinity they bind to that receptor.

- The μ (mu) receptor is the major analgesic opioid receptor and is found primarily in the brain, spinal cord, and gastrointestinal tract. Effects at this receptor include: analgesia, physical dependence, respiratory depression, miosis, euphoria, and reduced GI motility.^{7,8}

- The K (kappa) receptor is located in the brain, spinal cord, and peripheral sensory neurons. Effects at this receptor include: analgesia, anticonvulsant effects, depression, hallucinations, dysphoria, miosis, and sedation.
- The δ (delta) receptor is located in the brain and peripheral sensory neurons. Effects at this receptor include: analgesia, antidepressant effects, convulsant effects, and physical dependence.^{7,8}

The most common side effects associated with opioid use are: respiratory depression,

constipation, sedation, dysphoria, bradycardia, and nausea/vomiting.⁷ Some side effects can be predicted or avoided by understanding opioid binding affinities to certain opioid receptors. For example, the opioids morphine and fentanyl are strong agonists at mu receptors and have variable affinity at kappa and delta receptors. The opioid codeine has weaker affinity at mu receptors and virtually no affinity for kappa or delta receptors. Therefore, codeine at equianalgesic doses is less likely to cause respiratory depression, physical dependence, dysphoria, and hallucinations compared to morphine and fentanyl.⁷ Table 1 provides information on various opioids available.

Table 1: Opioid Products Available^{7,8}

<u>Generic name</u> <u>(Brand name)</u>	<u>Chemical Source</u>	<u>Route</u>	<u>a: Onset (minutes)</u> <u>b: Half-life(hours)</u>	<u>Comments:</u>
<i>Morphine-like agonists</i>				
Morphine (various)	Naturally occurring	IM PO	a: 10-20 min. b: 2-4 hrs.	-Drug of choice in severe pain
Hydro-morphone (Dilaudid, Exalgo)	Semisynthetic	IM PO	a: 10-20 min. b: 2-3 hrs.	-More potent than morphine
Oxymorphone (Opana, various)	Semisynthetic	IM PO	a: 10-20 min. b: 2 hrs.	-ER product to deter misuse
Hydrocodone (Norco, Vicodin)	Semisynthetic	PO	a: 30-60 min. b: 4 hrs.	-Use in moderate/severe pain -Most effective when combined with other products such as NSAIDs
Levorphanol (various)	Semisynthetic	PO	a: 30-60 min. b: 12-15 hrs.	-Use in severe pain
Codeine (various)	Naturally occurring	IM PO	a: 10-30 min. b: 3 hrs.	-Use in mild/moderate pain
Oxycodone (OxyContin, Oxecta, Roxicodone, various)	Semisynthetic	PO	a: 30-60 min. b: 2-3 hrs.	-Use in moderate/severe pain -CR formulation to deter misuse

<i>Mepiridine-like agonists</i>				
Meperidine (Demerol)	Synthetic	IM PO	a: 10-20 min. b: 2-6 hrs.	-Oral formulation not recommended -Use in severe pain
Fentanyl (Sublimaze, Duragesic, various)	Synthetic	IM Transdermal Buccal Transmucosal Sublingual Nasal inhaled	a: 30-60 min. b: 2-3 hrs.	-Use in severe pain -Transdermal should not be used for acute pain
<i>Diphenylheptanes</i>				
Methadone (Dolophine, various)	Synthetic	IM/IV PO	a: 30-60 min. b: 8-59 hrs.	-Effective for severe chronic pain -Sedation can be a major problem
<i>Partial agonists</i>				
Pentazocine (Talwin)	Synthetic	IM PO	a: 15-30 min. b: 2-3 hrs.	-Third-line agent for moderate-to-severe pain
Butorphanol (various)	Synthetic	IM Intranasal	a: 10-20 min. b: 3-4 hrs.	-Second-line agent for moderate-to-severe pain
Nalbuphine (various)	Synthetic	IM	a: <15 min. b: 5 hrs.	-Second-line agent for moderate-to-severe pain
Buprenorphine (Buprenex, Butrans, Subutex)	Synthetic	IM Transdermal Sublingual	a: 10-20 min. b: 2-6 hrs.	-Second-line agent for moderate-to-severe pain -Naloxone may not be effective for reversal
<i>Central analgesics</i>				
Tramadol (Ultram, Rybix, Ryzolt, ConZip)	Synthetic	PO	a: <60 min. b: 5-7 hrs.	-Dose reductions for elderly patients and those with renal impairment
Tapentadol (Nucynta)	Synthetic	PO	a: <60 min. b: 4 hrs.	-CR formulations to deter abuse

CLARIFICATION OF TERMINOLOGY SURROUNDING OPIOIDS

Opioid misuse, physical dependence, tolerance, and addiction are central concerns for healthcare professionals who are trying to effectively manage pain in their patients. These terms all have different meanings and are all frequently used incorrectly. It is important for both prescribers and pharmacists to have a clear understanding of the terminology surrounding opioids.

When opioids are taken chronically over an extended period of time, tolerance develops. Tolerance is the physiologic process where the body adjusts to a medication over time and higher doses are usually required to achieve the same desired effects.⁹

With opioids, tolerance is usually attributed to receptor downregulation. Basically, receptors become muted to a particular opioid dose overtime and certain effects are no longer seen. For example, respiratory depression and analgesia have a high degree of tolerance and occur at a faster rate than the effect of constipation, which is only minimally affected by tolerance.⁷ For patients taking opioids chronically, tolerance is an expected outcome and should not be linked to misuse or addiction.

Physical dependence to opioids is also erroneously linked to addiction. Physical dependence to opioids means that the body relies on an external source of opioids to prevent withdrawal symptoms. In normal circumstances, the body produces enough endogenous opioids (i.e. endorphins) to

prevent withdrawal symptoms such as: irritability, insomnia, hot/cold sweats, muscle aches/pains, and nausea. When opioids are taken chronically, the body stops producing endogenous opioids and relies on exogenous sources of opioids to keep withdrawal symptoms from occurring. This form of physical dependence is predictable and preventable and should not be confused with addiction. Withdrawal symptoms associated with physical dependence can be prevented by slowly reducing the intake of opioids and the dose. Other medications such as clonidine have also been used to reduce withdrawal symptoms when tapering is not effective.¹⁰

Unlike physical dependence and tolerance, addiction is abnormal. Addiction is defined as “a primary neurobiologic 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.”¹⁰ It is important to distinguish between addiction, physical dependence, and tolerance as they often occur together with opioid use. For example, people are dependent on food and water but are not addicted to them. If a patient is taking large doses of opioids, it is expected that he/she will develop tolerance and physical dependence overtime but not addiction. A person with opioid addiction experiences uncontrollable cravings and will use opioids despite harmful effects and regardless of pain. Table 2 highlights the components of addiction associated with opioid abuse.

Table 2: Components of Addiction⁹

<u>The Components of Addiction</u>	<u>Possible expression of patients on chronic opioids</u>
Loss of <u>C</u> ontrol	-Calls for early refills -Seeks opioids from other sources -Withdrawal symptoms noted frequently at appointments
<u>C</u> raving	-Increasing pain despite lack of progression of disease -Dismissive of non-opioid treatments -Recurring requests for increases in opioids
Use despite negative <u>C</u> onsequences	-Over sedation -Decreases in activity, functioning, or relationships -Disregardance of laws

OPIOID MISUSE

According to the Centers for Disease Control (CDC), the standard definition of misuse is defined as the use of prescription drugs in a manner other than as directed.¹¹ Other organizations such as the American Pain Society and the American Academy of Pain Medicine have expanded the definition to: “Any use of an illegal drug, and the intentional self-administration of a medication

for a nonmedical purpose such as altering one’s state of consciousness, ie. getting high.”¹² The term “misuse” is often used as an “umbrella term” because it is not possible to have addiction or substance abuse without it; however, opioid misuse can occur in individuals without addiction. Table 3 contains examples of situations of opioid misuse.

Table 3: Opioid Misuse Scenarios

<u>Opioid misuse scenarios</u>
<ul style="list-style-type: none"> ● Taking an opioid that is not prescribed to you ● Taking an opioid for a condition other than what it is prescribed for ● Taking a dose in a manner other than how it is prescribed <ul style="list-style-type: none"> ○ Crushing a tablet and snorting it ○ Taking more tablets than prescribed or more frequently than prescribed ● Taking an opioid to purposefully alter one’s mental function (ie. to get high)

According to the National Survey on Drug Use and Health (NSDUH), an estimated 4.3 million persons age 12 and over were current nonmedical users of prescription pain relievers in 2014.¹² Misuse of prescription painkillers was found to be most prevalent in young adults (age 18-25) and decreases as age

increases. Moreover, 1.4 million people misused prescription opioids for the first time for nonmedical uses in 2014.¹³

GUIDELINES

The best way for physicians and pharmacists to provide effective pain management and

promote patient safety is to use clinical practice guidelines. The American Pain Society and the American Academy of Pain Medicine are just two of the numerous associations that have created guidelines to assist practitioners in implementing safe and effective pain management plans in noncancer patients. While guidelines for cancer pain and end of life care are available and should be used in these situations, this population is much smaller than the noncancer population and is likely contributing minimally to the overall problem of opioid abuse. The guidelines published in 2009 started by helping physicians identify patients who may be at high-risk for opioid abuse and how to create pain management plans.

Recommendations on initiation, titration, and proper discontinuation of opioids make up the largest portion of the guidelines.

Recommendations for the prevention and management of adverse effects and managing breakthrough pain are also discussed in the guidelines. Experts believe that chronic pain can be managed in a safe and effective way when guidelines are used to prescribe opioids.¹⁴

The CDC is currently working on new guidelines aimed at improving the way opioids are prescribed for better and safer management of patients 18 and older with chronic pain.¹¹

PHARMACIST'S ROLE IN PAIN MANAGEMENT

Pharmacists play a critical role in the pain management process that involves both patient safety and adequate pain control. First, it is the pharmacist's responsibility to monitor every chronic pain patients' 5 As:^{15,16}

- **Analgesia:** Are the opioids reducing the patient's chronic pain?
- **Activities of daily living:** Are the opioids helping to improve functioning in daily activities?

- **Adverse effects:** Are the opioids causing intolerable adverse effects? Common ones to look at include: constipation, drowsiness, nausea/vomiting, altered mental status, depression, and endocrine abnormalities.
- **Aberrant behaviors:** Is there any evidence of abnormal or unusual behaviors? Examples include: frequent early refills, requests for opioids from multiple providers, abnormal urine drug screen, and abuse of alcohol or other drugs.
- **Affect:** Is the patient's behavior and mood appropriate?

When pharmacists have direct involvement in pain management, they are in a unique position to assist both patients and physicians. For example, a community pharmacist in Iowa offers adherence packaging for patients that are prone to substance abuse.¹⁷ After counselling chronic pain patients, he determines if packaging this patient's medication in a bubble pack would be beneficial. Just by reviewing the "5 As" with chronic pain patients, pharmacists can make a difference from helping the patient achieve appropriate analgesic effects to managing opioid-induced constipation.

Pharmacists are also acting as "gatekeepers" for opioid treatment agreements between physicians and patients. Treatment agreements contain both rules for patients on opioids (i.e. no early refills, mandatory drug screenings, no opioids from other prescribers, etc.) and expected outcomes from opioid treatment. When pharmacists have access to these treatment plans, they can monitor patient activity for aberrant behaviors and make sure opioids are working effectively to manage pain.¹⁸ In fact, many physicians are starting to see pharmacists as a team member in pain management. Pharmacists can alert prescribers to numerous different problems with opioid management. First, pharmacists

can check for drug interactions and make sure patients are on appropriate doses of opioids. The combination of opioids and benzodiazepines is the most common cause of polysubstance overdose deaths in the United States, an important drug interaction for pharmacists to alert physicians.³ Next, pharmacists can warn prescribers of potentials for aberrant behaviors. For example, prescribers may be unaware of multiple family members being on opioids or if opioids are being prescribed from other physicians. Pharmacists also typically see patients more than physicians and are more readily available for assisting with managing adverse effects such as constipation. Finally, pharmacists can assist prescribers with changing opioids by making sure the new dose of opioids is reasonable and safe. Pharmacists can help prevent withdrawal symptoms and adverse effects such as insomnia by making sure opioid dose conversions are calculated appropriately.

Pharmacists have a big role in managing chronic opioid use, and an even bigger role in keeping unused opioids out of the wrong hands. White House Office of National Rx Drug Control Policy Director Michael P. Botticelli stated, “since the majority of individuals who begin misusing prescription drugs get them from family and friends, we must make it easy to dispose of leftover drugs.” The DEA ruled in 2014 that community pharmacies are allowed to partner with local enforcement agencies in local take-back events to ensure proper medication disposal. Community pharmacies offer a less intimidating place than a police department for those who wish to dispose of unwanted medications.¹⁹ Even if community pharmacists do not hold drug take-backs at their own stores, they have a responsibility to inform patients on how to safely dispose of medications and the dangers of leaving opioids where children or pets have access.²⁰

GOVERNMENT INVOLVEMENT

The opioid epidemic has led to the passage of several laws at both the federal and state levels to try to combat opioid mortality. In an effort to reduce illicit opioid use, the Drug Enforcement Agency (DEA) moved all hydrocodone containing products to schedule II from schedule III. The Food and Drug Administration (FDA) has also approved changes affecting long-acting (LA) and extended-release (ER) opioid medications. First, manufacturers of LA or ER opioids are required to create provider education resources based on FDA blueprints. Prescribers of ER/LA formulations are encouraged, but not required to complete this self-education. Second, the FDA changed labeling on ER/LA formulations from “moderate to severe pain” to “For the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.”²¹ These are just a few of many changes. Many other government agencies are working diligently to come up with new regulations to combat the opioid epidemic.

As of 2014, 49 states and the District of Columbia have operating Prescription Drug-Monitoring Programs (PDMPs) to track patient prescriptions for controlled substances, including opioids. PDMPs have proven useful in reducing the availability of opioids, showing early signs of substance abuse, and showing the potential for drug interactions. However, PDMPs vary greatly from state to state and results are mixed. Only 21 states are mandating the use of PDMPs for opioid prescribers, leaving PDMPs as simply an optional, wasted resource. Many states are having an issue with real-time reporting and providing access to both prescribers and pharmacists. Furthermore, since PDMPs are state-run programs, information is only available for that particular state that a prescriber or pharmacist is currently located. The CDC is providing funding to expand and

improve PDMPs to include “universal, real-time reporting”. This expansion will provide pharmacists and prescribers the most current fill of an opioid, even across state lines.²¹

DRUGS FOR OPIOID ADDICTION

There are 3 classes of medications used today to help patients overcome opioid addiction:^{13,22}

- Opioid agonists (i.e. methadone) which activate opioid receptors
- Opioid partial agonists (i.e. buprenorphine) which activate opioid receptors but produce a blunted response
- Opioid antagonists (i.e. naltrexone) which block opioid receptors and interfere with rewarding effects of opioids

When used as a part of a specified treatment plan, these medications can effectively help patients refrain from taking other opioids, help combat withdrawal symptoms, and reduce risks associated with crime and infections. The American Society of Addiction Medicine (ASAM) published guidelines in 2015 addressing the use of methadone, buprenorphine, and naltrexone in opioid addiction.²²

Before a medication can be selected, a treatment venue must be selected. Opioid treatment programs (OTP) offer daily supervised dosing of methadone and possibly buprenorphine. Office-Based Opioid Treatment (OBOT) provides weekly or monthly prescriptions for buprenorphine only.²² Physicians offering OBOT must become certified via an eight-hour course and can only manage a maximum of 30 patients the first year and 100 patients any time after the first year.⁸ Naltrexone can be prescribed in any setting by any physician. For patients who require more supervision, OTP are often a better alternative to OBOT and may lead to

better outcomes.²²

Methadone is widely used in treating opioid addiction. Tolerance and physical dependence develop more slowly with methadone than with morphine and withdrawal symptoms are milder.⁷ Patients taking methadone for addiction should be seen on a daily basis and generally should be provided psychosocial and behavioral counseling.

Buprenorphine is best used in three stages: induction, stabilization, and maintenance. Induction is the first stage where patients are converted from an opioid of abuse to buprenorphine. The stabilization stage begins when a patient is no longer experiencing withdrawal symptoms or uncontrollable cravings. The maintenance stage is typically the longest stage and may last for life. This stage involves psychosocial and family counseling.^{8,22}

Naltrexone is best used in patients who are well past withdrawal symptoms and highly motivated to remain in recovery. Typically, it is not used in the initial stages of treatment, but may be used after methadone or buprenorphine.^{13,22}

While methadone, buprenorphine, and naltrexone have been used to successfully help people overcome addiction, relapse is a major concern. When patients taking these medications relapse, they require higher doses of opioids to produce desired effects and these higher doses may be lethal. Several organizations, including the CDC, are working to develop better plans and medications for opioid addiction.¹¹

NALOXONE

Naloxone is a potent, injectable medicine that can rapidly reverse an overdose due to prescription or illicit opioids by competitively antagonizing the μ -opioid receptor, ultimately dislodging opioids from their receptors in the brain to help rapidly reverse centrally

mediated respiratory depression and restore breathing that may have slowed or briefly stopped during an overdose, whether intentional or unintentional.^{4, 23,4} Naloxone has been an established antidote for opioid overdose for decades, with primary use among emergency department personnel and first responders such as paramedics.²⁴⁻²⁷ Unfortunately, access to naloxone for outpatient distribution is limited due to several barriers including:

- access to products
- funding and reimbursement
- legal barriers
- ethical issues
- the need for education at the level of the patient, the caregiver(s) or family, and provider.

Despite these hurdles, initiatives have been implemented regarding prevention strategies to reduce mortality associated with opioid overdose. Several US states have started outpatient naloxone dispensing to reduce opioid overdose-related deaths; however, there is limited exposure to this unique practice and limited appreciation for the role of a pharmacist within this clinical setting.

NALOXONE AUTO-INJECTOR

On April 3rd, 2014, the FDA approved Evzio, the first hand-held naloxone auto-injector to rapidly reverse opioid overdose specifically designed to be given by family members or caregivers. This single-dose injector is small enough to be carried in a pocket or stored in a medicine cabinet. It is intended for the emergency treatment of known or suspected opioid overdose, characterized by decreased breathing or heart rates, or loss of consciousness. Currently existing naloxone

drugs require administration via syringe and are most commonly used by trained medical personnel in emergency departments and ambulances. Evzio can be injected intramuscularly or subcutaneously. Once turned on, the device provides verbal instructions to the user describing how to deliver the medication. Family members or caregivers should become familiar with all instructions for use before administering to known or suspected persons to have had an opioid overdose. Family members or caregivers should also become familiar with the steps for using Evzio and practice with the trainer device, which is included along with the delivery device, before it is needed. Because naloxone may not work as long as opioids, repeat doses may be needed. Evzio is not a substitute for immediate medical care, and the person administering Evzio should seek further, immediate medical attention on the patient's behalf.²⁸

CONCLUSION

Pain is an unpleasant, subjective experience that affects millions of Americans. Not only does it impact the individual affected with the condition, it also places a huge burden on the patient's family and health care system. The assessment of pain requires a comprehensive assessment of signs and symptoms as well as suspected pain mechanisms. Pain relief, the ultimate goal, can be attained through the use of analgesics such as opioids; however, opioids are widely feared compounds due to their association with abuse, addiction, and other serious problems. Nevertheless, they are essential for the relief of pain and suffering in many pain cases, and healthcare professionals should be thoroughly educated on the proper use of these medications.

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