

PHARMACY SERVICES AND THE MANAGEMENT OF CHRONIC PAIN

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ABSTRACT

Pharmacists and pharmacy technicians are important resources for patients who need guidance when it comes to choosing pharmacological and non-pharmacological treatment options for pain. They can help with a patient's pain management in a number of healthcare environments, including hospital and commercial pharmacy settings. In many cases, the pharmacist is the most accessible member of a patient's medical team. When a pharmacist is involved in medication review, patient education, and medication prescribing, patient outcomes related to chronic pain management improve. Expanded roles for pharmacists in a patient's treatment options for chronic pain have also shown better outcomes for patients.

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How to Earn Credit: From March 12, 2022, through March 11, 2025, participants must:

- 1) Read the "learning objectives" and "author and planning team disclosures;"
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Educational Objectives: Upon completion of this educational activity, participants should be able to:

1. **Identify** the types and classifications of pain
2. **Describe** the pain assessment process
3. **Compare** pharmacotherapy to other pain management therapies that are available to patients

4. **Describe** the role of the pharmacist and pharmacy technician in a patient's pain management and their contribution to improving patient outcomes

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Introduction

Pain is a subjective experience, which means that patients will experience pain in diverse ways. This also means that there is no objective, physical methodology to measure pain. Pharmacists and pharmacy technicians have important roles to play in their patients' pain management in hospital and commercial pharmacy settings. When pharmacists interact with patients within these settings, they can facilitate patient education, and they can identify potential risks to patients who are part of specific population groups. Pharmacists and pharmacy technicians can be more effective in helping patients manage their pain when they utilize their knowledge of the physiology of pain and pain assessment. This knowledge is crucial for pharmacists and pharmacy technicians who may be reviewing a patient's medical history and records, and who may interact with primary care providers with the goal of improving outcomes for patients who have transient or persistent pain. Expanded roles for pharmacists in a patient's treatment options for chronic pain have also shown better outcomes for patients.

Defining Pain

Pain is a protective, physiological response to an event that has the potential to damage body tissue, or that may actually damage body tissue. This event is known as a "noxious stimulus."¹ Noxious stimuli are detected by nociceptors through transduction in their peripheral terminals, which causes the sensation called pain.² Nociceptive pain occurs from a "pin prick, touching something too hot or any potentially tissue damaging chemical, thermal or mechanical stimulus."²

The International Association for Study of Pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage."¹ Although pain is unpleasant, it is intended to cause a reaction in the person that will limit or avoid tissue damage.^{1,2}

A person experiences pain when three events occur: the person's nociceptive receptors are activated through transduction (as described

above); a message is then transmitted through the central nervous system; and, a pain response results.¹ When this system is functioning optimally, it serves the intended protective purposes of limiting further injury; however, this system can malfunction, resulting in sustained pain, pain resulting in spite of the absence of stimuli, and an amplification of pain signals, which are referred to as “central sensitization.”¹

Pain is a personal, subjective experience.^{2,3} Only the person experiencing pain can fully describe it. Because every person has a distinctive tolerance threshold, each person may measure pain differently. Factors that affect the experience of pain are multifactorial, and these will influence an individual’s tolerance to pain. These factors may be biological, psychological, or social.⁴ A patient’s medical history and treatment outcomes for pain can guide a health provider in developing a pain management plan for the patient.¹ As a consequence, pain is complex, and it can be difficult to manage.⁴

Types of Pain

There are distinct types of pain and they each respond differently to treatment methods. Pain is classified as either acute, subacute or chronic based on its duration.^{5,6} The type of pain, the patient’s perception of pain and the duration of pain are all included in the assessment of the patient’s condition and impacts pain management treatment.²

Acute pain occurs for a shorter duration and is classified as lasting for six weeks or less. Acute pain can be very brief, lasting for a few seconds or minutes before resolving. Subacute pain is the classification of pain that persists from seven to twelve weeks. It becomes chronic pain when the duration exceeds three months.⁵

Acute pain may be severe when the pain begins but often resolves completely with time and treatment. Acute pain causes a stress response, such as tachycardia and tachypnea, but this response typically ends when the pain is resolved, and the tissue has healed.⁶ Examples of situations where a patient may experience acute pain include surgery, burns, or skin lacerations.

Chronic pain lasts for a much longer period of time, and it may not be more tolerable than acute pain sensations. Longer lasting pain is not necessarily less debilitating than acute pain.⁷ Chronic pain that results from an injury can continue long after the precipitating condition has been treated. Favorable outcomes are sometimes judged by factors other than resolution of pain; for example, a patient may be considered recovered because the patient returned to work, even though the patient's pain persists.⁵

Chronic pain can desensitize the person experiencing it such that the pain no longer engages a stress response.⁷ A patient may be admitted for treatment that causes acute pain yet may already be suffering from chronic pain as well. A physiologic stress response may be developed due to acute pain from procedures or surgery, however, as the body's response to chronic pain continues concurrently, the patient may begin to adapt to it. In other cases, chronic pain can be very debilitating, resulting in comorbid conditions such as depression, irritability, and difficulties with sleeping.⁸ Examples of conditions that may result in chronic pain in addition to injury include autoimmune disorders (such as arthritis), certain types of cancer, or those of musculoskeletal dysfunction.^{2,6}

Physiological Classifications of Pain

Pain has been classified into three categories: (1) neuropathic pain, or pain that is experienced as numbness or tingling in the nervous system; (2) somatic pain, or musculoskeletal pain; and (3) visceral pain, or pain in the pelvis, ribs, or sternum.⁹

Neuropathic Pain

Neuropathic pain occurs when a person experiences pain related to changes in nerve fibers or their conductivity, usually resulting from a type of injury, lesion or disease of the somatosensory system.^{10,11} The somatosensory system has many receptor types throughout the body, such as thermoreceptors, mechanoreceptors, and chemoreceptors, which send signals

to the spinal cord and subsequently to the brain. Lesions within this system can cause altered or aberrant signaling to pain centers throughout the body, resulting in neuropathic pain.¹²

Neuropathic pain may be categorized by the presence or absence of co-existing conditions, and how the pain developed. Traumatic neuropathic pain causes the injured nerves to send incorrect pain signals to the brain, whether the injury to the body healed or not. An example of traumatic neuropathic pain is phantom limb pain, in which a person who has had an amputated limb continues to feel pain in the missing extremity.^{8,12}

Metabolic neuropathic pain occurs when a person experiences sensory pain as a result of complex medical disorders that affect the metabolic system, such as malnutrition or diabetes.¹³ One of the most common conditions causing metabolic neuropathic pain is diabetes mellitus. The patient with diabetes may suffer from nerve damage because of uncontrolled blood glucose levels, resulting in pain, numbness, burning, or tingling in the distal extremities. This type of pain is mechanistically dissimilar to other categories of pain syndromes such as those which result from inflammation. In an inflammatory cause of neurogenic pain, the etiology of pain is an alteration of chemical events where the inflammation is occurring and is both diagnosed and treated in a different manner.¹⁴

Infectious neuropathic pain develops from an infection in the body that causes nerve damage and subsequently, chronic pain that may be constant or intermittent. Examples of infections that can lead to neuropathic pain include varicella zoster virus that causes chickenpox and shingles which can lead to post-herpetic neuralgia; infection with Lyme disease or human immunodeficiency virus (HIV). The treatment of several of these disorders may itself cause pain which is indistinguishable from the disease itself, such as in HIV-induced neuropathy and antiretroviral toxic neuropathy.¹⁵

Immune-mediated neuropathies can cause autoimmune neuropathic pain. Chronic inflammatory demyelinating polyneuropathy occurs when the myelin sheath of the nerve fibers becomes damaged, resulting in pain in the

extremities. A multicenter study conducted by Pazzaglia, *et al.* (2011) reported that over 50% of patients with immune-mediated neuropathies had symptoms of neuropathic pain.¹⁶ Common descriptors of this type of neuropathic pain were paresthesias and spontaneous superficial pain. They also reported that conditions that were thought to be painless, as in multifocal motor neuropathy, did exhibit pain ranging from mild discomfort to overtly painful symptoms.¹⁶

Compression pain, also known as neuroma, is another type of neuropathic pain that occurs from many causes, such as swelling, inflammation, and muscle imbalance.¹ Examples of this type of pain include carpal tunnel syndrome and compartment syndrome.¹ Nerve injuries are often accompanied by musculoskeletal conditions, and medical conditions such as tendinitis, bursitis, or arthritis are caused by the same disorders associated with neuropathic pain.¹

Toxic substance exposure can result in neuropathic pain.¹⁷ Chemicals such as lead, mercury, arsenic, thallium, lithium, chemotherapy drugs, antibiotics, such as isoniazid and metronidazole, and some cardiovascular medications, including amiodarone and statins can all cause neuropathic pain with exposure.¹⁸⁻²⁰

Somatic Pain

Somatic pain is the most prevalent pain present in cancer patients.⁹ Somatic pain symptoms tend to be a more localized, aching pain.²¹ Nociceptive receptors are stimulated, and this can evoke somatic pain when these nerve endings send pain messages to the brain because of cell injury to body areas containing connective tissue.⁶ Somatic pain is pain that occurs in areas such as the bones, joints, muscles, or the skin. It may be further classified as *cutaneous* somatic pain and *deep* somatic pain. In cases of bone metastases, nociceptors are sensitized by prostaglandins and osteoclast-activating factors, which result in hyperalgesia and pain. Drugs are selected that inhibit nociceptor sensitization and bone pain and may possibly inhibit tumor growth.⁶

Cutaneous somatic pain often develops in superficial tissues from injuries that are less traumatic to the body. The patient may describe this sensation as sharp or burning.²² Examples of injuries that can cause cutaneous pain include skin abrasions. Deep somatic pain is described as occurring beneath the cutaneous level and often caused by trauma to bones or muscles resulting in more intense pain. Deeper, somatic pain injuries may manifest as bone fractures or torn ligaments.²³

Visceral Pain

Visceral pain is that which is affected by internal organs and tissues, such as the heart, gastrointestinal system, or the kidneys, and signals nociceptors within them to respond to painful stimuli. The pain may develop as part of a disease process, which results in cramping or tissue spasms, or in ischemia development at the site. Visceral pain may also occur as a result of injury, or through some type of medical procedure, during which the organs and tissues are moved, stretched, or manipulated, resulting in pain.²¹

Visceral pain may be difficult to localize because the pain may be initiated at one site in the body and radiate to another area. With radicular pain, it may be difficult to determine the initial location of the pain and whether an injury has occurred. More than 20% of the population suffer from chronic visceral pain.²⁴ Visceral pain is sometimes described as cramping, squeezing, or a feeling of pressure. The intensity of the pain may also vary from mild and intermittent discomfort to severe and agonizing pain.¹⁰

Pain Assessment

Health providers should assess a patient's pain by reviewing a patient's medical history, description of pain, and past successes of pain relief. A pharmacist's involvement in assessing a patient's pain management plan has been shown to improve a patient's health outcomes.⁴

Pain assessment includes evaluating a patient's total needs, taking into consideration the patient's physical, psychological, and emotional matters. A

patient in pain may have other complications and issues that need to be managed as part of care, such as difficulties with eating, problems with concentration, impaired mobility, and constipation due to pain medications. The location and source of pain can significantly impact a patient's abilities to perform tasks, even the activities of daily living.^{8,25}

In a clinical setting, assessing pain may be just as important as assessing blood pressure, heart rate, and other vital signs. Some experts view pain assessment as "the 5th vital sign."²⁶ Other experts disagree but regardless of a clinician's opinion on this subject, pain assessment is crucial enough for a patient's well-being that it should be given the same priority as other vital sign measurements. Pain assessment should occur at regular intervals to ensure that there is adequate pain management.

Patients in pain are in a vulnerable state and they often do not voice the presence of pain or its severity. Reasons for this include not wanting to be labeled as drug seeking, or as a complainer, and still others do not want to disturb their healthcare providers. They may believe that pain is a normal part of hospitalization and may not feel the need to vocalize it. There are people who feel that expressing pain is too personal and they do not wish to share that part of themselves, remaining stoic. Finally, some patients do not notify their health clinicians that they are having pain because they fear a diagnostic outcome, such as a new condition requiring narcotics, or an examination precipitating additional tests. Because there are so many reasons why patients may not disclose their symptoms, health clinicians need to assess pain so that it can be appropriately managed.

The perception of pain is affected by several factors unique to each patient. A patient's pain threshold, cultural background, expectations for pain management, and previous experiences with pain all impact the patient's responses to a current pain syndrome. These factors should also be recognized as impactful to a patient's response. Psychosocial factors should also be recognized. Pain catastrophizing can be defined as "an exaggerated negative mental set brought to bear during actual or anticipated painful experience."¹⁹ Increased fear of pain is also associated with higher levels of self-reported

experimentally induced pain intensity. Both may be an influence on pain assessments.¹⁹ Two of the most common causes of unrelieved pain among patients are inadequate pain assessment measures and failure to act on a patient's report of pain.

Adequate pain assessment involves determining the location, intensity, and duration of the patient's pain based on responses, either verbal or observed. Providing adequate pain control means acting on those responses to provide effective relief, and to continue monitoring therapy to determine if additional measures are needed.^{8,25}

Location

Pain location is the site as described by the patient, which may or may not be the actual origin of the symptom. If the patient is experiencing radicular pain, it may be experienced at both the site of origin as well as the region to which pain is emanating.^{8,25} When a patient experiences an injury such as an upper extremity fracture, pain may be felt at the site of the fracture, but also throughout the entirety of the limb. Alternatively, referred pain occurs when the source of the pain is in one part of the body, but the patient feels pain in a completely different area. An example of referred pain is a myocardial infarction that does not produce chest pain; instead, pain is felt in the left arm and neck. Referred pain most commonly occurs in situations where a patient is experiencing visceral pain.²⁷

To determine where the patient is feeling pain, the clinician should ask the patient to point to the site of pain, rather than only asking the patient for a description. A body diagram may also be useful for some patients to point to affected areas and can be particularly helpful if a patient is experiencing pain in more than one location, and to alert a clinician to the possibility of chronic widespread pain, a sign of increased pain sensitization.²⁸ If the patient has an injury that is apparent, such as a wound or contusion at a specific site on the body, it would seem logical that this point is the location of the patient's pain. Despite having an obvious injury, the patient still needs to specify where the pain is located. There may be more than one location of pain, which could

indicate another injury, or the patient may be feeling pain associated with a different condition that is unrelated to the obvious injury.²⁷

Duration

Duration of pain as a classification seems self-explanatory; however, it is a consideration not only of the current pain episode, but also any precipitating factors. A patient may have been participating in certain activities that initially caused the pain; for example, developing chest pain while jogging which stops when exercise concludes. The differential diagnosis could be anginal symptoms or costochondritis or even gastric reflux. The fact that it starts and stops with a specific activity is important to the diagnostic work up.

A patient may know the exact time when the pain started and be able to relate precisely how long the occurrence lasted. A description of pain duration also includes whether the pain is constant or intermittent; in the latter, the patient should try to describe the intervals and the length of time between episodes of pain. If the patient is currently between pain intervals, it is helpful to learn how long it has been since a painful episode last occurred.

Description

Careful attention must be paid to the type of words the patient uses to describe pain. At times, it may be difficult for the patient to come up with the words or an appropriate description of the type, intensity, or location of pain. There are some tools available that clinicians may use to help the patient use the right words to describe pain.

The OLD CARTS mnemonic can be used to help a patient to describe the location and intensity of pain. The mnemonic is used as follows:²⁹

- Onset: when did the pain start or how long has it been going on?
- Localized: where is the pain?
- Description: explain how the pain feels: burning, aching, sharp, stabbing, throbbing

- Characteristics: describe the pain's intensity
- Aggravating: is there anything that makes the pain worse?
- Relief: what factors would improve the pain or provide pain relief? What treatments have been provided for the pain; what was the effect?
- Time: how long have you had the pain and has it been constant or intermittent?
- Symptoms: has the pain had an impact on any other of your daily activities, such as eating, sleeping, or mood?

A simpler method of describing pain intensity would be for the clinician to assess whether the patient is having pain and if the pain could be described as *mild, moderate, or severe*.³⁰ This pain assessment tool may need to be used in conjunction with assessment of nonverbal signs that indicate pain severity, *e.g.*, grimacing.³¹ Pain can also cause sleep disturbances, decreased self-esteem, diminished social interactions, irritability, a lack of interest in eating, and confusion or impaired thinking.³²

In addition to assessing pain severity, location, and duration, part of the pain assessment process is asking patients about their perception of pain.³¹ A patient may have a complete understanding as to why pain is occurring, such as post-operatively. However, there are those that lack an understanding as to the cause of the pain they are experiencing. They may believe that they are experiencing pain because they did something wrong, or, if they have referred pain, they may not understand why the pain is not located at the source of the injury or illness. Asking patients what is known about their pain provides an opportunity for education about how the body processes injuries or illness and may better explain why some procedures or treatments are necessary.

Clinicians should also be aware that a patient's perception of pain may go beyond an obvious related disorder or physiologic process. Exploring what pain means to the patient by incorporating physiological and psychological issues, such as depression and anxiety, will allow for a fuller understanding of the cause of pain and the appropriate therapy needed. Of the general population, about 5% are affected by depression, but this percentage is

greatly increased by those suffering with chronic pain. Estimates are that between 30-45% of chronic pain patients also have depression. There are studies explaining the relationship between pain and depression to be of bidirectionality. Depression is a positive predictor of the development of chronic pain, and chronic pain increases the risk of developing depression.³³ This points to the importance of distinguishing the varied perceptions people have of pain. The psychological components of how suffering, loss of function, decreased ambulation and the fear of death impact a patient need to be included in a comprehensive pain assessment.

Methods for Assessing Pain

There are numerous methods for assessing pain. They include the numerical rating scale, and the Wong-Baker FACES pain rating scale.

Numerical Rating Scale

The numerical rating scale is one of the most commonly used methods for assessing a patient's pain.³⁴ Because pain cannot be objectively measured but instead relies on a patient's admission of pain level, this type of scale can adequately explain the level of intensity the patient is experiencing in a method that is easy to understand.

The numerical rating scale is appropriate to use for most adult inpatients who are cognitively aware and able to respond. The numerical rating scale asks the patient to rate pain on a scale of 0 to 10.³⁴ A score of 0 means the patient has no pain, while a score of 10 is the worst pain imaginable. The patient gives a number somewhere on the scale to describe the current level of pain.³⁴

Some facilities assess a patient's pain tolerance upon admission by explaining the numeric rating scale and asking not only what the patient's current level of pain is, but also what number would be an acceptable level of discomfort. For example, a patient may rate pain felt at a '7' on the numeric rating scale but may also say that the pain can be tolerated as a '2.'³⁴ For this

patient, a level of pain described as a '2' may be quite tolerable, while some other patients may tolerate pain classified as a '6' and others may only be comfortable at a level of '0.' Understanding the patient's *tolerable* level of pain can guide clinicians to know whether pain management measures are working and whether the patient is being kept comfortable.

It is helpful to relate pain tolerability in relation to functional ability. Approximately 1/3rd of post-operative older patients reported pain that was "painful but bearable" with a numeric rating of 5/10, while over 50% of older adults reported it as merely "bothersome pain." It may be stated by the patient that "I can stand the pain, it's not that bad" followed by a refusal of pain medication.³⁵

FACES Rating Scale

Other assessment measures are available for some patients who cannot speak but who are cognitively aware. The Wong-Baker FACES pain rating scale has a series of faces with different expressions that may explain how much pain a person is having. At one end of the scale, the equivalent of a '0' on the numeric rating scale, the face is smiling and appears happy, indicating no pain. Moving down the scale, the expressions of the faces become progressively sadder or appear to be having more pain. At the opposite end of the scale in the position of '10' on the numeric rating scale, the face is crying and appears to be in significant pain. The patient who cannot talk can use this type of pain scale to point to which face most closely resembles their level of pain. The Wong-Baker FACES scale may also be used for children ages 3 and older, however, this scale is not recommended in older adults due to its original intent to be a scale for children. There are happy faces rather than neutral expressions, and some show tears on faces, which has been stated to be problematic in getting some adults, such as stoic men and women, to use the full scale. The "animated cartoonish faces are said to be less appealing to adults."³⁵

Assessing Pain in Cognitively Impaired Patients

Pain may be difficult to assess among patients who are cognitively impaired and who have difficulty expressing their level of pain on a numerical scale. A study by Jones, *et al.* (2019) was undertaken to quantify the impact of cognitive impairment on pain assessment and management practices in the emergency department.³⁶ They determined that those patients with cognitive impairment were less likely to have their pain assessed using a standardized tool and 9.4% more likely to be assessed using ad hoc methods only (95% confidence interval 4.6-19.1) They determined that pain is inadequately and inappropriately assessed for elderly patients with a cognitive impairment in the emergency department, which resulted in delays initiating pain management.³⁶ If patients are unable to express their pain effectively, it is important to assess for visual signs of pain in the patient and to provide pain relief measures if the patient is showing nonverbal cues indicative of pain. These cues might include fidgeting, grimacing, crying, moaning, being aggressive or disruptive, rocking, or pacing. Additionally, physiological changes may also be present, even if the patient is unable to describe being in pain. Signs include an increased heart rate, increased respiratory rate, increased blood pressure, dilated pupils, or sweating.

Assessing Pain in Children and Adolescents

Walco, Kopecky, Weisman, *et al.* (2018) reported that there were over “35 self-report pain intensity measures designed for children and adolescents;”³⁷ however, the reliability and validity of most of these tools are not adequately supported by evidence.³⁷ These tools vary when it comes to responsiveness and what may be interpreted from the assessment. Reliability and validity also vary across pediatric age groups. An in-depth discussion on pediatric, self-report, pain measurement tools is beyond the scope of this course, but Walco, Kopecky, Weisman, *et al.*, provide a useful overview of the effectiveness of some of the scales as applied to different age groups.³⁷

Assessment Based on Cultural Considerations

A healthcare provider should consider the role cultural or ethnic backgrounds may play in a patient's sensitivity to pain, or a patient's willingness to discuss pain with his or her provider. For example, Rhudy, *et al.* (2020) found that Native Americans may be more pain sensitive based on their finding that Native Americans had lower cold pain thresholds or tolerances than non-Hispanic Whites.³⁸ This suggests possible pain risk differences between Native Americans other U.S. minority groups.³⁸ Awareness of possible cultural or ethnic differences can improve patient outcomes from pain management treatments.

Pharmacotherapy

Beyond performing adequate pain assessments, it is important to provide appropriate treatment based on the patient's description of their level of pain. It is never enough just to assess and document a patient's pain; essential components of clinical pain care and pain relief must be afforded to the patient through medication and adjuvant therapies.

The concept of pain management means providing treatment for a patient's pain to eliminate the pain or reduce it to a level that is tolerable. In many outpatient or inpatient situations, this is accomplished using pharmacotherapy: medications are prescribed for pain relief and a schedule of medication delivery is maintained. Clinicians will need to use evidenced-based decisions and clinical judgment to determine whether a type of pain medication will be effective and if it is probable to cause too many adverse effects. In some cases when a medication is to be given *as needed* instead of on a set schedule, clinical judgment must be used about the appropriate medication schedule, as well as when to hold back from administering medication, depending on the patient's condition.

Opioid Pain Medications

Opioids are medications given to provide pain relief by binding to certain receptors in the spinal cord, which then block the perception of pain in the brain.³⁹ Opiates may be produced from natural substances, or they may be synthetic, and they are not the same as narcotics, although the two terms may be used interchangeably. Opioid medications are used specifically for pain control because of their action, while narcotics may be used for other purposes beyond pain relief.

The clinician always keeps in mind that the most effective opioid treatment will be the least amount to cause the best pain relief; providing adequate dosages to control pain while minimizing negative effects, such as sedation, respiratory depression, or confusion that may develop with these drugs. Among hospitalized patients, opioid medications are the most common types of drugs given to control pain.⁴⁰

Opioid analgesics are powerful pain relievers frequently used for patients suffering from significant pain. In order to prescribe opioids, the clinician must provide sufficient medication to provide effective pain management, all the while considering the potential for addiction, abuse, diversion, potential overdoses, and misuse of the drug.^{39,41}

Types of Opioids

There are three types of opioids: agonists, agonist-antagonists, and partial agonists.⁴² Full agonists work in a manner similar to endorphins in the body and increasing amounts of these drugs continue to increase pain control and sedation levels. Examples of full agonist opioid drugs include morphine, codeine, and hydromorphone.⁴²

Agonist-antagonist analgesic medications work by blocking some nerve receptor sites while stimulating others. If a patient is already taking an opioid analgesic, an agonist-antagonist medication may reduce its effectiveness.³² However, these drugs can be very effective for use without other opioid

medications in place. They have a ceiling effect which means that giving higher or more frequent doses will not necessarily continue to produce more pain relief. Examples of agonist-antagonist medications include butorphanol tartrate (Stadol®) and nalbuphine hydrochloride (Nubain®).^{43,44}

Partial agonist medications, like agonist-antagonist medications, also have a ceiling effect and so their use is similarly limited.⁴⁵ However, these drugs may be used when other opioid medications are not available or in cases when a patient is unable to take other kinds of medications for pain relief. Partial agonist medications work by blocking certain nerve receptor sites while binding to others. An example of this medication is buprenorphine (Buprenex®).⁴⁵ Buprenorphine has been used as one of the drugs to treat addictions to opioid medication.⁴⁵

Opioids are highly addictive, and the prescription of long- and short-acting opioids has been regulated, increasingly so within the past five years. Limits as to quantity prescribed have been legislatively controlled to cut down on the number of patients becoming addicted to prescription medication and to reduce the number of opioid overdoses. The use of buprenorphine, the opioid in Suboxone (brand) was developed as a safer opioid for the treatment of pain.⁴⁶ As a partial opioid agonist-antagonist, this drug has inherent abuse deterrence properties; it is used in the treatment of opioid addictions. As a long-acting, high-affinity partial agonist at the mu-opioid receptor, buprenorphine prevents withdrawal and craving and stabilizes opioid receptors. The most common formulation is buprenorphine and naloxone (Suboxone) in a 4:1 ratio.⁴⁷

Routes of Administration

The route of administration directly impacts a drug's onset and absorption.⁴⁸ For example, a drug administered orally will be exposed to first-pass metabolism as it makes its way through the gastrointestinal tract, whereas a transdermal patch avoids this exposure.⁴⁸ The route of administration also impacts the risk that a particular drug will be misused. A

“drug with high bioavailability upon oral or intranasal administration will achieve higher plasma concentration and is more likely to be [misused].”⁴⁸

There are several means of delivery of opioid medications, so the selection for administration is based on a patient’s condition and the ease of taking the medication.⁴⁸ The oral route is preferable among patients who must take opioid medications on a long-term basis. It is the easiest and least expensive method of administration and can be used among patients who are conscious, can swallow, and who do not have gastrointestinal issues that would preclude its action.⁴⁸

Some patients who cannot take medication by mouth may receive drugs through the rectal route. Morphine and hydromorphone are available as rectal suppositories.⁴⁹ Not all patients tolerate this route, and it is not usually considered as a first choice for most people. It should also not be used among patients who have diarrhea or those with breakdown in or around the anus and rectum. However, rectal administration of medications can be effective for those with limited alternative routes for taking medication, and the drugs are usually absorbed relatively quickly through the intestinal mucosa. Fentanyl is available in the transdermal form. This method involves placing a patch on the skin and the medication is slowly absorbed.⁵⁰ It can provide analgesia for up to 72 hours, but it may take several hours before effective analgesia levels are achieved.⁵¹

Other methods of administration of opioid medications that are more invasive include subcutaneous, intramuscular, intravenous, and intraspinal routes.⁴⁸ Subcutaneous administration involves injecting the medication with a needle into the subcutaneous fat under the surface of the skin. The injection can only be given in certain locations, such as the abdomen or upper arm, where the patient is more likely to have fatty tissue present, as compared to other areas. The intramuscular route also involves injecting medication into the patient, but the needle must be longer, and the injection goes much deeper into muscular tissue. Common areas used are the deltoid muscle of the upper arm and the ventrogluteal muscle of the hip. Because this method

of administration can be quite painful for the patient, it is often avoided in favor of other routes.⁵²

Intravenous (IV) administration involves injecting medication directly into a patient's vein. The patient must first have an IV line in place. This route can be quick and effective and can be used on patients who would otherwise have difficulty taking medications in other methods, including patients who are unconscious.⁴⁸ The intrathecal (intraspinal) method of administration involves injecting medication into a catheter that has been placed in the epidural space of the spine.^{53,54} This method may be used for patients who need long-term analgesia as an alternative to other routes.^{53,54}

Patient-controlled Analgesia

Patient-controlled analgesia (PCA) is a process that was developed to allow a patient to have more control over pain by self-administering doses of medication through a pump delivery system.^{55,56} The patient has an intravenous line for fluids and medication administration and is connected to the PCA pump.^{55,56} The pump contains a syringe with the prescribed medication in it, which is set to deliver a specific amount of medication to the patient when a button is pushed. Some settings offer a basal or continuous dose and the patient can supplement the pain pump when the need for more pain relief occurs. In other situations, the PCA is set up to give occasional doses of pain medication when the patient needs pain relief.^{55,56}

A PCA intravenous pump can reduce the need for the patient to depend on the clinician to administer pain medication. At times, it may be difficult to administer pain medication in a timely manner in an acute care setting before pain becomes uncontrolled for the patient. With the PCA, the patient can push a button to deliver pain medication when pain is felt, potentially stopping it before it worsens. The PCA pump is set to deliver only a certain amount per hour so that the patient does not receive too much.^{55,56} It will lock out so that even if the patient continues to push the button to deliver additional medication, more medication will not be received. This safety feature prevents accidental overdose of opioid medications.

Patients typically use the PCA for themselves, without someone else pushing the button to deliver medication for them. The safety in this feature is that if the patient becomes sedated after receiving a bolus of medication, more medication will not be received. The most common medications used with PCA include morphine, fentanyl, and hydromorphone.^{55,56} The setup of the PCA is typically a clinical duty that requires proper staff training to change the medication syringe when it becomes empty. Use of the PCA does not eliminate the need for continued assessment and patient monitoring.^{55,56} The clinician must still assess the patient's level of pain to determine if the PCA is providing adequate pain relief. If the clinician sets up the PCA, the settings should be checked with another staff member to determine that they are correct and to avoid accidental opioid overuse or toxic dosing.

Non-opioid Pain Medications

Non-opioid analgesics are drugs that are typically used for mild to moderate pain relief.⁵⁷ These medications may be provided for patients by prescription when in the hospital; they may also be bought over the counter. There is a ceiling as to how much analgesia these drugs can provide, so giving more or repeating doses to increase comfort may not be effective or safe.⁵⁸

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) are medications such as ibuprofen or aspirin. These drugs provide mild to moderate pain relief, they reduce inflammation, and they can help to control high fever. Patients who take these drugs may be at higher risk of bleeding, as they can have an anticoagulant effect. Other side effects of NSAID use are gastrointestinal irritation or bleeding and acute renal failure.⁵⁹ NSAIDs work by blocking an enzyme known as cyclooxygenase (COX), which is needed for creating prostaglandins, the substances in the body that initiate pain signals. Cyclooxygenase may be classified as COX-1 or COX-2, and each type may be inhibited by different medications.^{57,60} For example, aspirin and ibuprofen are COX-1 inhibitors, while celecoxib (Celebrex®) is a COX-2 inhibitor. The Food and Drug Administration has since grouped all NSAIDs, whether COX-2

inhibitor NSAIDs or non-selective NSAIDs, into one class with similar warnings regarding skin, cardiovascular, renal, and gastrointestinal side effects.⁵⁹

Acetaminophen

Acetaminophen is another non-opioid analgesic that is effective for reducing mild to moderate pain and as a fever reducer.⁵⁷ Acetaminophen does not have the same anti-inflammatory effects as NSAIDs; however, NSAIDs may lead to gastrointestinal bleeding, which is less likely with acetaminophen.⁵⁷⁻⁶⁰

Non-opioid analgesics as an Alternative to Opioids

Martinez, *et al.* (2017) studied the outcomes from patients who were administered acetaminophen, combined with NSAID, or with nefopam. These combination drugs were found to be “superior to most analgesics used alone in terms of reducing morphine consumption with PCA. Three analgesics used alone (α -2 agonists, NSAIDs and COX-2 inhibitors) were the most efficient, with tramadol and acetaminophen the least efficient.”⁵⁷

Adjuvants

Other medications may be combined with analgesics to provide more effective pain control. Adjuvant medications, also called co-analgesics, are those that are not designed for analgesia when they are used as a monotherapy; however, when they are combined with opioid or non-opioid analgesic, there can be a greater effect of pain relief. The World Health Organization (WHO) has designed a pain control ladder to guide clinicians toward choosing and administering medications for pain relief.⁵⁸ The WHO recommends combining medications such as adjuvants and opioid analgesics to provide more effective relief when compared to using one type of analgesic at a time. Therefore, if possible, the patient can derive better pain relief when medications are administered in combination.⁵⁸

Antidepressants may be used in combination with analgesics for better pain control. Tricyclic antidepressants can affect how pain is perceived by interfering with the reuptake of the neurotransmitters serotonin and norepinephrine in the brain. An example of a tricyclic antidepressant that may be used as a co-analgesic is amitriptyline (Elavil®). Medications normally used as anticonvulsants may also be beneficial as co-analgesics. Anticonvulsants may work well as adjuvant therapy because they suppress neuron firing for seizure control, which may also be helpful for some types of pain, particularly neuropathic pain. Examples of these types of drugs include gabapentin and carbamazepine.⁶¹

In addition to analgesics, other drugs may also be used as adjuvant therapy because their effects can reduce or eliminate symptoms commonly associated with pain. Corticosteroids may be administered with analgesics to reduce swelling or inflammation, and to reduce pain.⁶² Benzodiazepines, typically prescribed to manage anxiety, depression, or insomnia, may also be prescribed as part of pain management. When combined with analgesics, benzodiazepines can help to reduce muscle spasms that may accompany pain.⁶³

Other Modes of Administering Pain Medication

Epidural Analgesia

Epidural analgesia involves administering medications for pain control into a catheter that has been placed in the epidural space within the spinal column.⁶⁴⁻⁶⁶ Side effects of epidural analgesia are often associated with the effect the catheter has on specific nerves or are local reactions to just having the catheter in place. With an epidural, the patient is at higher risk of bradycardia, hypotension, and respiratory depression.⁶⁷ Opioid medications administered through the epidural may cause side effects of nausea and vomiting. Patients often complain of widespread itching, and there is a risk of developing a rash.⁶⁸

Nerve Block

A nerve block is a pain control measure that involves injecting medication into a specific nerve in order to anesthetize a specific part of the body.⁶⁹ The nerve block is performed prior to a procedure or treatment to cause the area to become sufficiently desensitized for the patient to not feel any pain associated with treatment or for a period of time afterward. Anesthesia providers typically administer nerve blocks, but the responsibility for caring for the patients with the blocks requires clinical care to ensure adequate pain relief is maintained. Most nerve blocks are placed as peripheral blocks, as they are designed to control pain for one part of the body, such as an extremity. They are most often used to control pain in procedures affecting the arms, shoulders, knees, ankles, feet, or hips.⁶⁹

Alternative Therapies for Pain Control

There are nonpharmacological therapies for pain management that may be helpful when used in addition to or in place of pharmacologic therapy. These methods may impact the body through physical means or may use cognitive or behavioral therapy to help the patient manage pain through psychological measures.^{70,71} Nonpharmacologic measures that may be used for pain control may include psychotherapy, massage, heat or cold (thermal) therapy, and transcutaneous electrical nerve stimulation.

Massage Therapy

Massage involves kneading or manipulating the muscles and tissues under the skin to promote relaxation and stress relief.⁷² Pain can cause the muscles to contract and tighten, causing additional pain and muscular tension. The massage practitioner rubs and manipulates the musculature, most commonly in the back, shoulders, arms, and legs. This results in improved circulation to the tissues and greater relaxation and tension release.⁷²

Thermal Therapy

Thermal therapy involves the application of warm or cold packs to various sites on the body and may be used in areas where a patient is feeling pain.⁷² This process may also include warm baths, heating pads, or ice massage. Application of these measures can help with pain relief by assisting the body with tissue repair.⁷² Heat therapy increases circulation to the affected site, which can increase range of motion, improve joint stiffness, and relax the muscles. Alternatively, cold therapy reduces the amount of blood flow to a site and may reduce swelling of injured tissues. By decreasing circulation to an affected area, cold therapy can also reduce inflammation.⁷²

Transcutaneous Electrical Nerve Stimulation (TENS)

Transcutaneous electrical nerve stimulation (TENS) activates a complex neuronal network to reduce pain by “activating descending inhibitory systems in the central nervous system to reduce hyperalgesia.”⁷³ A TENS unit is a physical therapy modality that delivers alternating electric current through the application of cutaneous pads (electrodes) placed over the area where the patient is experiencing pain. It activates large diameter afferent nerve fibers which when sent to the central nervous system can reduce pain if applied at the strongest intensity possible while the patient remains comfortable. This is critical for the success of the treatment, as lower intensities are ineffective.⁷³ The modality delivers electrical current through the electrode, stimulating the muscle fibers to regulate nociceptive impulses responsible for sending pain messages. TENS may also cause an increase in release of endorphins, which can also help the patient to feel better.⁷³ Effective analgesia for chronic pain conditions may be limited due to developing tolerance to TENS. This is expected if there are daily repeated applications at the same frequency, intensity, and pulse duration.⁷³

Psychotherapy and Mind-body Exercises

Psychotherapies, such as cognitive-behavioral therapy, may improve patient outcomes for resolving chronic pain. These therapies may be done as

monotherapies or in combination with physiotherapy.⁷¹ There are mind-body exercises that can be taught to a patient, which can change responsiveness to pain. If there is any intervention that causes a change in a patient's mental or emotional response which correspondingly makes changes in the body, it can be called a "mind-body" intervention.⁷⁴ This methodology is used to alter the patient's perception of the pain experience. The measures do not always relieve pain, but rather assist the patient in the ability to form new adaptations when pain is felt. Pain can cause the affected person to experience stress, depression, or anxiety, which may further compound the feelings of pain. Utilizing mind-body techniques may help to regulate the emotional responses which the patient has become accustomed to feeling when pain is experienced.^{74,75}

Mind-body techniques cause an alteration of a maladaptive neurophysiologic pathway, leading to a more positive reaction to pain, interrupting the tendency to secondarily experience depression and anxiety. A study of veterans was undertaken by Cosio and Swaroop in 2016 to determine the differential impact that mind-body medical interventions have on psychological distress among veterans with chronic pain, not caused by cancer.⁷⁴ They used primarily two techniques, that of Cognitive Behavioral Therapy and Acceptance and Commitment Therapy. The conclusion of the study was that both mind-body medical interventions for chronic pain showed a decrease in anxiety reported by the veterans and provided evidence of the treatment effectiveness of both interventions for chronic pain.⁷⁴

Distraction is a psychological intervention in which a patient who is in pain focuses on something other than the pain. When concentrating on something else, a distracted patient may actually become unaware of the pain.⁷⁶ Distraction can be through visual methods, such as watching television or reading a book; auditory measures, as in listening to music, or a physical distraction, such as massage or deep breathing techniques.⁷⁶

Other examples of mind-body methodologies to help with pain control include relaxation, mindfulness, biofeedback, and cognitive-behavioral therapy. Relaxation techniques help the muscles to relax, reducing tension

and producing an opposite effect of the fight-or-flight response.^{75,76} Studies have shown that the relief from anxiety and low baseline depression were the most important predictors for pain relief and the most strongly associated with functional improvement, so these techniques are very relevant for better outcomes.⁷⁷

One relaxation technique is progressive muscle relaxation, in which the patient actively concentrates on tensing and then relaxing certain muscle groups. Laughter can be a form of relaxation therapy that can improve a patient's mood and how the individual responds to pain. These methods have also been shown to reduce inflammation and make the brain respond more to endorphins.^{75,76}

Mindfulness is a form of distraction where the patient focuses on other thoughts beyond pain. Zhang, *et al.* (2019) recited a definition of mindfulness that described it as "nonjudgmental attention to the present moment."⁷⁸ This approach can reduce the amount of emotional reaction that often goes along with pain, helping a patient focus on life and the activities around the patient's pain. Zhang, *et al.*, further reported that an eight-week mindfulness meditation training could effectively regulate mood and reduce anxiety and depression.⁷⁸ Mindfulness-related health benefits are associated with enhancements in mechanisms supporting cognitive control, emotion regulation, positive mood, and acceptance.⁷⁹

Mindfulness meditation could be such a suitable narcotic-free pain therapy as it has been repeatedly found to decrease chronic pain symptomologies. This form of meditation attenuates pain through unique psychological and neural processes; and it has recently been demonstrated to be more effective in reducing pain than placebo without engaging endogenously driven opioidergic systems to do so.⁸⁰

Biofeedback involves using thoughts to control certain body functions; for example, biofeedback might involve using thought processes to slow a racing heart rate.⁸¹ Biofeedback requires focus of attention toward making a change in the body. A patient can utilize the measurement of certain bodily

functions, such as blood pressure readings or by using a heart rate monitor, and then relax and focus the mind to intentionally change these functions.⁸¹ It is a relaxation process of learning to control the sympathetic nervous system, thereby reducing stress and tension that can contribute to pain.

The Role of Pharmacists and Pharmacy Technicians in Pain Management

Pharmacists and pharmacy technicians have an important role to play in their patients' pain management.^{4,82} In a number of settings, the pharmacist is the most accessible member of a patient's medical team.⁸¹ When a pharmacist is involved in medication review, patient education, and medication prescribing, patient outcomes related to chronic pain management improve.⁸² This coincides with patient expectations who appear to want greater interaction and information from their pharmacist, than what is typically provided by them.⁸² "Training and education may help pharmacists to better engage in patient-centered care when interacting with people living with persistent pain, thereby improving health outcomes for these patients."⁸²

Giannitrapani, *et al.* (2018) reported on the complex issues faced within the Veterans Health Administration because its population experiences "high rates of chronic disease, including pain and other comorbid conditions."⁴ In order to address these issues, Giannitrapani, *et al.*, proposed that the role of clinical pharmacists could be expanded to include authority to prescribe pain medications and order medication renewals. Pharmacists could also educate patients about medications, take a greater role in reviewing state prescription drug monitoring programs, and reassess and monitor patients. All of this may be done by a pharmacist in the context of a patient's overall opioid therapy management.⁴

Pharmacists may also be further involved in primary care by utilizing "population management activities."⁴ An example of population management could include a pharmacist or pharmacy technician reviewing a patient population group as a whole in order to identify if that group is at higher risk of opioid misuse or other pain management concern in advance.⁴ Greater

involvement by pharmacists in a patient's pain management has resulted in a decreased burden on other primary care professionals and improved patient outcomes.⁴ Giannitrapani, *et al.*, concluded by stating: "Interdisciplinary collaboration and communication between the medicine and pharmacy services will be essential to successful clinical pharmacist role expansion and shared team prioritization."⁴

Pharmacists and pharmacy technicians should also be aware of potential barriers for healthcare workers that may interfere with proper pain management for patients. According to Lau, *et al.* (2019), pharmacists reported that the most common barrier to a pharmacist providing care was their patients being non-receptive to interacting with them. A strategy proposed to overcome this barrier was for the pharmacist to show empathy for patients, and build rapport through communication.⁸² Other barriers may include a lack knowledge regarding pain assessment tools, a patient's inability to communicate his or her pain, and a prescription for pain medication that has been prescribed without a full evaluation of a patient's pain score.⁸³ Pharmacists and pharmacy technicians who review a patient's medical history and records, and who interact with primary care providers, may be able to alleviate these barriers and improve a patient's outcomes for pain management.

Summary

Pain is a personal, subjective experience, and the person experiencing pain should describe it in their own terms to include intensity but also co-occurring symptoms and the impact of pain on activities of daily life. Pain must be understood as being whatever the person experiencing it describes it to be. Health clinicians must rely on the patient's description of pain, either verbally or through the aid of a pain assessment tool, as well as the patient's report of the efficacy of pain relief measures.

Types of pain and their treatment have been presented in the above sections. A challenging aspect of pain is when it becomes chronic due to tissue and nerve damage. The perception of pain becomes influenced by many

factors related to physiological and psychosocial factors. Pain types and degrees of pain combined with other comorbidities and their treatments, such as in the example of chemotherapy or radiation therapy for cancer, can significantly impair a patients' quality of life.

Pain therapies specific to the patient's diagnosis aimed at alleviating pain involve medications, pain management procedures, and alternative type treatments such as massage and mindfulness. It is strongly recommended that the best approach is to utilize the resources of an interdisciplinary team that may include medical, rehabilitation, and psychiatric services working together to promote safe and appropriate pain management treatment and patient recovery.

Pharmacists and pharmacy technicians are important resources for patients who need guidance when it comes to choosing pharmacological and non-pharmacological treatment options for pain. In many cases, the pharmacist is the most accessible member of a patient's medical team. When a pharmacist is involved in medication review, patient education, and medication prescribing, patient outcomes related to chronic pain management improve. Expanded roles for pharmacists in a patient's treatment options for chronic pain have also shown better outcomes for patients.

Course Test

- 1. Which of the following is an example of traumatic neuropathic pain?**
 - a. Compartment syndrome
 - b. Diabetic neuropathy
 - c. Varicella zoster virus
 - d. Phantom limb pain

- 2. _____ pain is the most prevalent pain present in cancer patients.**
 - a. Psychosomatic
 - b. Visceral
 - c. Cutaneous
 - d. Somatic

- 3. A patient is diagnosed with an acute myocardial infarction. The patient has only felt pain in his jaw (no chest pain). This is an example of**
 - a. referred pain.
 - b. receptive pain.
 - c. radiating pain.
 - d. random pain.

- 4. Which of the following is an example of a full agonist opioid?**
 - a. Morphine
 - b. Buprenex
 - c. Elavil
 - d. Nubain

- 5. Which of the following is an example of a pharmacist or pharmacy technician engaged in a "population management activity"?**
 - a. Reviewing patient records to determine if the pharmacy is treating all population groups equally
 - b. Engaging in interdisciplinary collaboration and communication
 - c. Reviewing a patient population group to determine if that group is at higher risk of opioid misuse
 - d. Engaging in continuing education in the area of pain management

6. _____ is a psychological intervention in which a patient who is in pain focuses on something other than the pain.

- a. Referral
- b. Biofeedback
- c. Distraction
- d. Relaxation

7. True or False: Pharmacists have reported that a common barrier they face to providing care to patients was their patients' non-receptive attitude to interacting with them.

- a. True
- b. False

8. The numerical rating scale explains the _____ of pain a patient is experiencing in a method that is easy to understand.

- a. type
- b. intensity level
- c. complexity
- d. duration

9. _____ is a non-opioid analgesic that is effective for reducing mild to moderate pain.

- a. Nalbuphine hydrochloride
- b. Hydromorphone
- c. Acetaminophen
- d. Buprenorphine

10. True or False: Because of its adverse effects profile, fentanyl is not used in patient-controlled analgesia drug delivery systems.

- a. True
- b. False

11. Adjuvant medications are drugs that are

- a. contraindicated for use with analgesics.
- b. used as an alternative pain reliever to opioids.
- c. used before administering analgesics.
- d. not designed for analgesia as a monotherapy but can enhance pain relief when combined with an analgesic.

- 12. _____ can affect how pain is perceived by interfering with the reuptake of the neurotransmitters serotonin and norepinephrine in the brain.**
- a. Amitriptyline
 - b. Gabapentin
 - c. Carbamazepine
 - d. Acetaminophen
- 13. Anticonvulsants may work well as adjuvant therapy because they suppress neuron firing for seizure control, which may also be helpful for some types of pain, particularly**
- a. nociceptive pain.
 - b. visceral pain.
 - c. neuropathic pain.
 - d. somatic pain.
- 14. Heat therapy should be used for a patient who wants to**
- a. increase circulation to a body site.
 - b. reduce the amount of blood flow to a site.
 - c. relieve gastrointestinal disorders.
 - d. reduce inflammation.
- 15. Nonsteroidal anti-inflammatory drugs work by blocking an enzyme known as _____ which is needed for creating prostaglandins.**
- a. carboxylase
 - b. urease
 - c. cyclooxygenase
 - d. acetylcholine

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