



Section I:

Background and Significance

A. INTRODUCTION

After years of neglect, issues of pain assessment and management have captured the attention of both health care professionals and the public. Factors that prompted such attention include the high prevalence of pain, continuing evidence that pain is undertreated, and a growing awareness of the adverse consequences of inadequately managed pain.

Pain is common. About 9 in 10 Americans regularly suffer from pain,¹ and pain is the most common reason individuals seek health care.² Each year, an estimated 25 million Americans experience acute pain due to injury or surgery and another 50 million suffer chronic pain.^{3,4} Chronic pain is the most common cause of long-term disability, and almost one third of all Americans will experience severe chronic pain at some point in their lives.⁵ As the population ages, the number of people who will need treatment for pain from back disorders, degenerative joint diseases, rheumatologic conditions, visceral diseases, and cancer is expected to rise.⁵

Pain is often undertreated. Improved understanding of pain mechanisms has advanced treatment for pain. Sufficient knowledge and resources exist to manage pain in an estimated 90% of individuals with acute or cancer pain.⁶ Safe and effective medical treatment for many types of chronic

pain also is available.⁷ Yet recent studies, reports, and a position statement^{2,8-9} suggest that many types of pain (e.g., postoperative pain, cancer pain, chronic noncancer pain) and patient populations (e.g., elderly patients, children, minorities, substance abusers)¹⁰⁻¹¹ are undertreated. Data from a 1999 survey suggest that only 1 in 4 individuals with pain receive appropriate therapy.^{4,12}

Inadequate pain management has adverse consequences. The adverse consequences of undertreated pain are considerable. Poorly managed acute pain may cause serious medical complications (e.g., pneumonia, deep venous thrombosis), impair recovery from injury or procedures, and/or progress to chronic pain.¹³ Undertreated chronic pain can impair an individual's ability to carry out daily activities and diminish quality of life.¹⁴ In addition to disability, undertreated pain causes significant suffering. Individuals with poorly controlled pain may experience anxiety, fear, anger, or depression.¹⁵ Pain is also a major cause of work absenteeism, underemployment, and unemployment.² Mounting health care costs and disability compensation reflect, in part, poor care for pain-related conditions.¹⁶ Thus, undertreated pain has significant physical, psychological, and financial consequences.

The undertreatment of pain is not a new problem. The Agency for Health Care Policy and Research (AHCPR)^a published the first clinical practice guideline (CPG) for pain management in 1992. The authors of this guideline acknowledged the prior efforts of multiple health care disciplines (e.g., surgery, anesthesiology, nursing) and pain management groups (e.g., American Pain Society, International Association for the Study of Pain) to address this situation.¹³ Multiple groups have subsequently produced CPGs that address the management of many types of pain. The recently introduced Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards for pain assessment and management¹⁷ represent a giant step forward in improving pain management.^b

To facilitate these efforts, this monograph has two primary objectives: 1) to provide practical knowledge that will enhance the reader's understanding and management of pain and 2) to introduce some strategies to improve pain man-

Learning Objectives

After reading this monograph, the participant should be able to:

1. Describe the current status of pain management in the United States, barriers to appropriate assessment and management of pain, and consequences of undertreatment of pain.
2. Explain the pathophysiologic mechanisms involved in pain perception.
3. Name elements of the pain assessment process, a tool used for pain assessment, and strategies for overcoming barriers to pain assessment.
4. List the types of pharmacotherapies used to manage pain and compare the mechanisms of action, uses, dosage forms, routes of administration, dosages, and side effects of the various options.
5. Discuss the role of nonpharmacologic interventions in treating pain and name a clinical use for a nonpharmacologic treatment.

^a The Agency for Health Care Policy and Research is now the Agency for Healthcare Research and Quality.

^b These JCAHO standards first appeared in the 2000-2001 JCAHO standards manual and apply to ambulatory care, behavioral health, managed behavioral health, health care networks, home care, hospitals, long-term care organizations, and pharmacies.

agement (e.g., CPGs, standards), as further explored in monograph 2. Due to the breadth and complexity of the subject matter, a comprehensive discussion of all aspects of pain assessment and management is beyond the scope of this monograph. The scope and potential limitations of this monograph are as follows:

- The neurological and psychological mechanisms that underlie pain are complex, and knowledge of mechanisms is limited. The discussion of pathophysiology in this monograph emphasizes practical knowledge that will facilitate diagnosis and/or the selection of appropriate interventions.
- Controversy exists over how both pain and analgesics should be classified. This monograph reviews only a few of the many classification systems.
- Various factors (e.g., insufficient funding for studies, lack of good diagnostic codes) limit the availability of current, reliable epidemiological data related to pain.
- A host of factors, including the setting, characteristics of the pain, and patient factors (e.g., age, medical condition, language and cognitive abilities) influence pain assessment. This monograph provides an overview of pain assessment, but primarily focuses on the initial assessment.
- Many strategies exist to manage various types of pain. This monograph reviews pharmacologic and nonpharmacologic treatments for pain, with greater emphasis on the former. Specific information about the treatment of certain conditions is limited to some common and treatable types of pain. Coverage of treatment issues relevant to special populations (e.g., children, the elderly) is limited.
- The discussion of pharmacologic treatments emphasizes: 1) the major classes of drugs used for pain management; 2) examples and salient features of these drugs; and 3) some means of ensuring the safe, strategic, and effective use of these agents. However, this information is only an overview. The reader should consult CPGs for specific guidance in managing patients.
- Due to the large volume of associated literature, a review of the mechanisms, assessment, and management of pain associated with some conditions (e.g., cancer) is beyond the scope of this monograph. This monograph focuses on the pathophysiology, epidemiology, assessment, and treatment of acute pain and chronic noncancer pain (CNCP).

B. DEFINITIONS AND MECHANISMS OF PAIN

This section of the monograph explores mechanisms that underlie the perception of pain. It also reviews a pain classification system based on underlying pathophysiology. The goal is to provide practical information that will facilitate pain assessment and management. A question-and-answer format is used to provide information about the following:

- The definition of pain
- The process by which noxious stimuli generate neural signals and the transmission of these signals to higher centers (nociception)
- The role of inflammatory mediators, neurotransmitters, and neuropeptides in these processes (i.e., targets of many pharmacologic therapies)
- Definitions and causes of some clinical pain states
- Underlying mechanisms and characteristics of somatic pain, visceral pain, and neuropathic pain.

1. What Is Pain?

In 1968, McCaffery defined pain as “whatever the experiencing person says it is, existing whenever s/he says it does”.¹⁸ This definition emphasizes that pain is a subjective experience with no objective measures. It also stresses that the patient, not clinician, is the authority on the pain and that his or her self-report is the most reliable indicator of pain.¹³ In 1979, the International Association for the Study of Pain (IASP) introduced the most widely used definition of pain. The IASP defined pain as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”¹⁹ This definition emphasizes that pain is a complex experience that includes multiple dimensions.

2. How Does Injury Lead to Pain?

Nociception refers to the process by which information about tissue damage is conveyed to the central nervous system (CNS). Exactly how this information is ultimately perceived as

painful is unclear. In addition, there can be pain without nociception (e.g., phantom limb pain) and nociception without pain. But classic descriptions of pain typically include four processes:²⁰⁻²³

- **Transduction:** the conversion of the energy from a noxious thermal, mechanical, or chemical stimulus into electrical energy (nerve impulses) by sensory receptors called nociceptors
- **Transmission:** the transmission of these neural signals from the site of transduction (periphery) to the spinal cord and brain
- **Perception:** the appreciation of signals arriving in higher structures as pain
- **Modulation:** descending inhibitory and facilitatory input from the brain that influences (modulates) nociceptive transmission at the level of the spinal cord.

3. What Happens During Transduction?

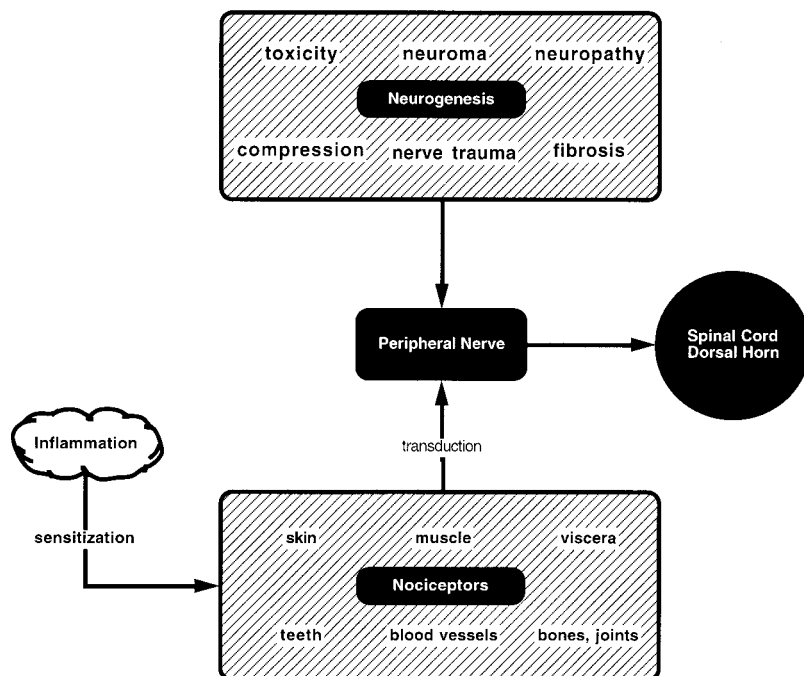
a. Nociceptor activation and sensitization

Nociceptors are sensory receptors that are preferentially sensitive to tissue trauma or a stimulus that would damage tissue if prolonged.¹⁹ These receptors are the free endings of (primary afferent) nerve fibers distributed throughout the periphery (Figure 1). Signals from these nociceptors travel primarily along two fiber types: slowly conducting unmyelinated C-fibers and small, myelinated, and more rapidly conducting A-delta fibers^c (Figure 2).

Injury to tissue causes cells to break down and release various tissue byproducts and mediators of inflammation (e.g., prostaglandins, substance P, bradykinin, histamine, serotonin, cytokines).^{24,25} Some of these substances activate nociceptors (i.e., cause them to generate nerve impulses) and

^cIn addition to these nociceptors, A-beta fibers (which normally subserved touch) sometimes act as nociceptors when sensitized. The functioning of nociceptors depends upon the electrophysiological properties of the tissues, co-factors, and cytokines.²⁴

Figure 1.



Source: Reference 22.

Peripheral origins of pain. Noxious signaling may result from either abnormal firing patterns due to damage or disease in the peripheral nerves or stimulation of nociceptors (free nerve endings due to tissue trauma). Inflammation in injured or diseased tissue sensitizes nociceptors, lowering their firing thresholds. Some clinical pain states have no peripheral origin, arising from disorders of brain function.

most sensitize nociceptors (i.e., increase their excitability and discharge frequency).^{26,27} Ongoing activation of nociceptors may cause nociceptive pain (see I.B.9). Peripheral (nociceptor) sensitization amplifies signal transmission and thereby contributes to central sensitization and clinical pain states (see I.B.7-8).²⁸

b. Peripheral neuropathic pain

Not all pain that originates in the periphery is nociceptive pain. Some neuropathic pain is caused by injury or dysfunction of the peripheral nervous system (i.e., peripheral nerves, ganglia, and nerve plexi)(see I.B.10)(Figure 1).²²

c. Clinical implications

Some analgesics target the inflammatory process that produces sensitization. For example, nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX), thus decreasing

the synthesis of prostaglandins.²⁹⁻³⁰ Other analgesics (e.g., antiepileptic drugs, local anesthetics) block or modulate channels, thus inhibiting the generation of nerve impulses.

4. What Is Transmission?

Nerve impulses generated in the periphery are transmitted to the spinal cord and brain in several phases:^{21,31}

a. Periphery to the spinal cord

Most sensory nerve impulses travel via the nerve processes (axons) of primary afferent neurons to the dorsal horn (DH) of the spinal cord (Figure 2).³² There, primary afferent neurons propagate nerve impulses to DH neurons through the release of excitatory amino acids (EAAs) (e.g., glutamate, aspartate) and neuropeptides (e.g., substance P) at synapses (connections) between cells.^{4,39} Activated DH projection neurons forward nociceptive impulses toward the brain.

However, not all events in the DH facilitate nociception. Spinal interneurons release

⁴The excitatory amino acids (EAAs) glutamate and aspartate mediate most excitatory transmission in the CNS, including that related to nociception.³³ The neuropeptide substance P activates spinal neurons and enhances their responsiveness to EAA, thus also facilitating nociception.³⁴⁻³⁸

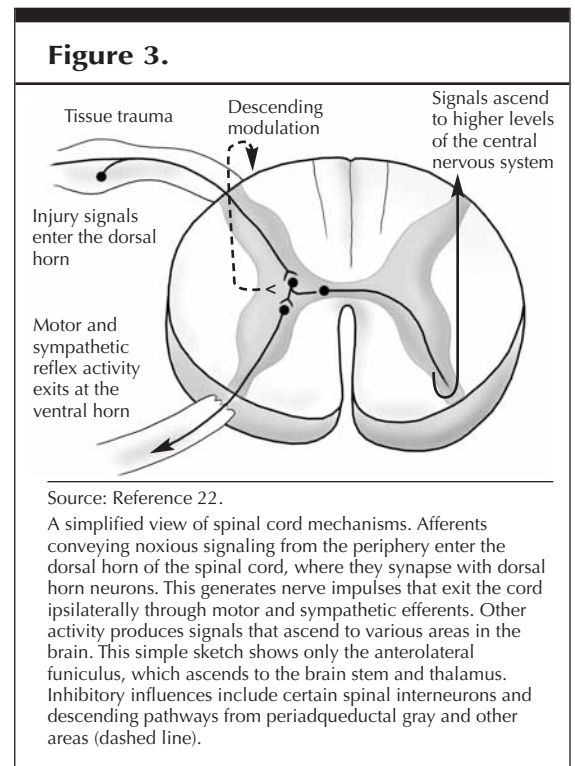
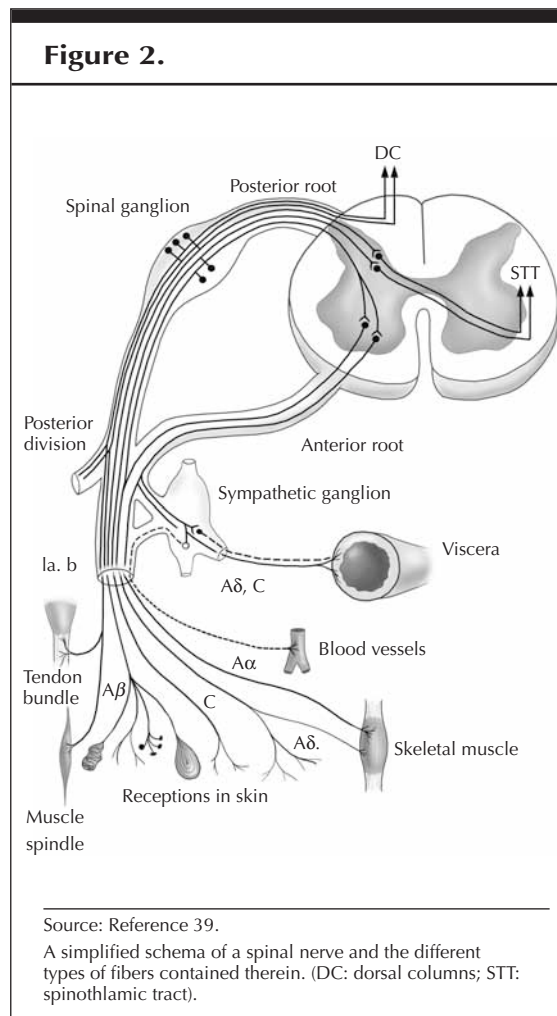
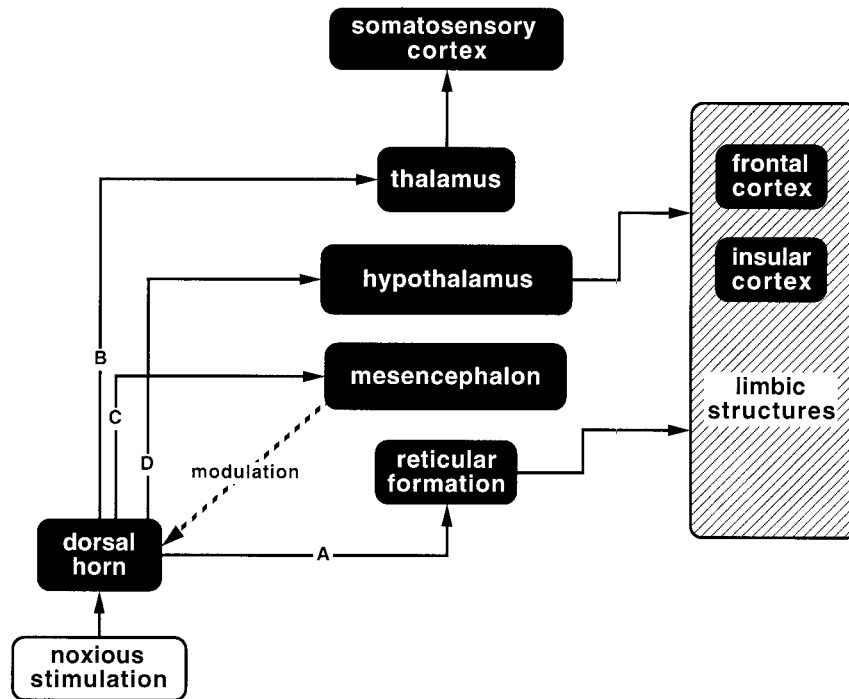


Figure 4.



Source: Reference 22.

Multiple pathways of nociceptive transmission for the spinal cord to central structures. There are four major pathways, the A: spinoreticular; B: spinothalamic; C: spinomesencephalic; and D: spinohypothalamic tracts.

inhibitory amino acids (e.g., γ -aminobutyric acid [GABA]) and neuropeptides (endogenous opioids) that bind to receptors on primary afferent and DH neurons and inhibit nociceptive transmission by presynaptic and postsynaptic mechanisms.³⁹⁻⁴² Descending inhibitory input from the brain also modulates DH nociceptive transmission (see I.B.6) (Figure 3). Thus, nociceptive traffic in the DH is not merely relayed to higher centers but rather is heavily modulated. These inhibitory events are part of a natural nociceptive-modulating system that counterbalances the activity of the nociceptive-signaling system.

b. Spinal cord to the brain

The nerve processes of DH projection neurons project to the brain in bundles called ascending tracts. Projection neurons from some DH regions transmit nociceptive signals to the thalamus via the spinothalamic tract (STT) (Figures 2, 4).^{39,43} Others transmit nociceptive information to the reticular formation, mesencephalon, and hypothalamus via the spinoreticular, spinomesencephalic, and spinohypothalamic tracts (Figure 4).^{22,44}

c. Clinical implications

Some analgesics inhibit nociception in the DH. For example, opioid analgesics bind to opioid receptors on primary afferent and DH neurons and mimic the inhibitory effects of endogenous opioids. They also bind to opioid receptors in the brain and activate descending pathways that further inhibit DH nociceptive transmission.⁴⁵ Baclofen, a GABA agonist, binds to GABA_B receptors and mimics the inhibitory effects of GABA on nociceptive transmission.⁴⁶

5. What Is Perception?

The perception of pain is an uncomfortable awareness of some part of the body, characterized by a distinctly unpleasant sensation and negative emotion best described as threat. Both cortical and limbic system structures are involved.⁴⁷ Nociceptive information from some DH projection neurons travels via the thalamus to the contralateral somatosensory cortex³⁹ (Figure 4), where input is somatotopically mapped to pre-

serve information about the location, intensity, and quality of the pain.^{43,48} The thalamus relays other nociceptive input to the limbic system.⁴⁴ This input joins input from the spinoreticular and spinomesencephalic tracts to mediate affective aspects of pain.²⁰ Immediate social and environmental context influences the perception of pain, as do past experience and culture. Consequently, a standard cause of pain (e.g., surgery) can generate enormous individual differences in pain perception.

6. What Is Modulation?

a. Descending pathways

Modulation of nociceptive transmission occurs at multiple (peripheral, spinal, supraspinal) levels. Yet, historically, modulation has been viewed as the attenuation of DH transmission by descending inhibitory input from the brain. Melzack and Wall's Gate Control Theory brought this notion to the forefront in 1965.⁴⁹ Models of descending pain systems now include both inhibitory and facilitory descending pathways.

Multiple brain regions contribute to descending inhibitory pathways.³⁹ Nerve fibers from these pathways release inhibitory substances (e.g., endogenous opioids, serotonin, norepinephrine, GABA) at synapses with other neurons in the DH. These substances bind to receptors on primary afferent and/or DH neurons and inhibit nociceptive transmission. Such endogenous modulation may contribute to the wide variations in pain perception observed among patients with similar injuries.^{20,50-51}

b. Clinical implications

Some analgesics enhance the effects of descending inhibitory input. For example, some antidepressants interfere with the reuptake of serotonin and norepinephrine at synapses, increasing their relative interstitial concentration (availability)⁵²⁻⁵³ and the activity of endogenous pain-modulating pathways.^{21,50,53a} Thus, some, but not all, antidepressants are used to treat some types of chronic pain.

7. What Is Peripheral Sensitization?

Inflammatory mediators, intense, repeated, or prolonged noxious stimulation, or both can sensi-

tize nociceptors.^{26,54-55} Sensitized nociceptors exhibit a lowered threshold for activation and an increased rate of firing.^{25,56-57} In other words, they generate nerve impulses more readily and more often. Peripheral (nociceptor) sensitization plays an important role in central sensitization and clinical pain states such as hyperalgesia (increased response to a painful stimulus) and allodynia (pain caused by a normally innocuous stimulus).⁵⁸⁻⁵⁹

8. What Is Central Sensitization?

a. Definitions and features

Central sensitization refers to a state of spinal neuron hyperexcitability.⁶⁰ Tissue injury (inflammation), nerve injury (i.e., aberrant neural input), or both may cause it,²⁷ and ongoing nociceptive input from the periphery is needed to maintain it.⁴⁸ Repeated stimulation of C-nociceptors initially causes a gradual increase in the frequency of DH neuron firing known as "wind-up."⁶¹ Activation of N-methyl D-aspartate (NMDA) receptors^e plays a key role in this process.^{27,64-65} The clinical correlate of wind-up-temporal summation-refers to a progressive increase in pain experienced over the course of a repeated stimulus.⁶⁶

Repeated or prolonged input from C-nociceptors or damaged nerves causes a longer-lasting increase in DH neuron excitability and responsiveness (i.e., central sensitization^f)^{67,75} which may outlast the stimulus by minutes to hours.³⁸ Central sensitization is associated with a reduction in central inhibition, spontaneous DH neuron activity, the recruitment of responses from neurons that normally only respond to low-intensity stimuli (i.e., altered neural connections), and expansion of DH neuron receptive fields.^{27,60,67,76-78} Clinically, these changes may manifest as: 1) an increased response to a noxious stimulus (hyperalgesia), 2) a painful response to a normally innocuous stimulus (allo-

^eEarly transient changes include removal of the voltage-dependent magnesium blockade of NMDA receptors. This permits glutamate to activate NMDA receptors, with subsequent temporal summation of slow synaptic potentials that manifests as wind-up.^{27,62-63}

^fCentral sensitization reflects a complex series of changes that may begin with the release of excitatory substances (e.g., glutamate, substance P) from cells following noxious stimulation. These substances activate NMDA and non-NMDA (NK) receptors, which increases intracellular calcium levels⁶⁷⁻⁷⁰ and activates calcium-dependent intracellular kinases.^{38,71} These kinases break down arachidonic acid (releasing byproducts)⁷² and phosphorylate ion channels and NMDA receptors. Potential consequences of these changes include altered synaptic transfer and gene expression (e.g., c-fos).^{27,60,73-74} Collectively, these changes may promote long-lasting increases in DH neuron excitability (i.e., central sensitization).

dynia), 3) prolonged pain after a transient stimulus (persistent pain), and 4) the spread of pain to uninjured tissue (i.e., referred pain).^{60,79} In contrast to hyperalgesia caused by peripheral mechanisms (i.e., primary hyperalgesia), such secondary hyperalgesia extends beyond the region of injury.^{48,80}

b. Clinical implications

Sensitization is likely responsible for most of the continuing pain and hyperalgesia after an injury.⁸¹ This sensitivity may be due to “normal” noxious input from injured and inflamed tissue or “abnormal” input from injured nerves or ganglia. In the former case, sensitization serves an adaptive purpose. That is, the hyperalgesia and allodynia encourage protection of the injury during the healing phase. However, these processes can persist long after healing of the injury in the setting of chronic pain.

Central sensitization plays a key role in some chronic pain, especially pain induced by nerve injury or dysfunction (i.e., neuropathic pain). It explains why neuropathic pain often exceeds the provoking stimulus, both spatially and temporally.^{48,60} Central sensitization also explains the long-standing observation that established pain is more difficult to suppress than acute pain.^{13,75,82-83}

In contrast to nociceptive pain, neuropathic

pain is often unresponsive or poorly responsive to NSAIDs and opioids.⁸⁴⁻⁸⁵ However, it may respond to antiepileptic drugs, antidepressants, or local anesthetics.⁸⁶

9. What Is Nociceptive Pain?

Pain that is classified on the basis of its presumed underlying pathophysiology is broadly categorized as nociceptive or neuropathic pain.⁸⁷ Nociceptive pain is caused by the ongoing activation of A- δ and C-nociceptors in response to a noxious stimulus (e.g., injury, disease, inflammation).⁸⁸ Pain arising from visceral organs is called visceral pain, whereas that arising from tissues such as skin, muscle, joint capsules, and bone is called somatic pain. Somatic pain may be further categorized as superficial (cutaneous) or deep somatic pain (Table 1).

In contrast to neuropathic pain, the nervous system associated with nociceptive pain is functioning properly. Generally, there is a close correspondence between pain perception and stimulus intensity, and the pain is indicative of real or potential tissue damage. Differences in how stimuli are processed across tissue types contribute to the pain’s varying characteristics (Table 1).²² For

Table 1. Examples and Characteristics of Nociceptive Pain

	Superficial Somatic Pain	Deep Somatic Pain	Visceral Pain
Nociceptor location	Skin, subcutaneous tissue, and mucous membranes	Muscles, tendons, joints, fascia, and bones	Visceral organs ^a
Potential stimuli	External mechanical, chemical, or thermal events Dermatologic disorders	Overuse strain, mechanical injury, cramping, ischemia, inflammation	Organ distension, muscle spasm, traction, ischemia, inflammation
Localization	Well localized	Localized or diffuse and radiating	Well or poorly localized
Quality	Sharp, pricking, or burning sensation	Usually dull or aching, cramping	Deep aching or sharp stabbing pain, which is often referred to cutaneous sites
Associated symptoms and signs	Cutaneous tenderness, hyperalgesia hyperesthesia, allodynia	Tenderness, reflex muscle spasm, and sympathetic hyperactivity ^b	Malaise, nausea, vomiting, sweating, tenderness, reflex muscle spasm
Clinical examples	Sunburn, chemical or thermal burns, cuts and contusions of the skin	Arthritis pain, tendonitis, myofascial pain	Colic, appendicitis, pancreatitis, peptic ulcer disease, bladder distension

Sources: References 22-24 and 88-89.

^aVisceral organs include the heart, lungs, gastrointestinal tract, pancreas, liver, gallbladder, kidneys, and bladder.

^bSymptoms and signs of sympathetic (autonomic) nervous system hyperactivity include increased heart rate, blood pressure, and respiratory rate; sweating; pallor; dilated pupils; nausea; vomiting; dry mouth; and increased muscle tension.

example, cutaneous pain is often described as a well-localized sharp, pricking, or burning sensation; deep somatic pain, as a diffuse dull or aching sensation; and visceral pain, as a deep cramping sensation that may be referred to other sites (i.e., referred pain).⁸⁸ Associated clinical pain states (e.g., hyperalgesia, allodynia) reflect sensitization (see I.B.7-8).^{88,90}

10. What Is Neuropathic Pain?

Neuropathic pain is caused by aberrant signal processing in the peripheral or central nervous system.⁹⁶ In other words, neuropathic pain reflects nervous system injury or impairment. Common causes of neuropathic pain include trauma, inflammation, metabolic diseases (e.g., diabetes), infections (e.g., herpes zoster), tumors, toxins, and primary neurological diseases.⁸¹ Neuropathic pain can be broadly categorized as peripheral or central in origin.⁹⁶ Painful peripheral mononeuropathy and polyneuropathy, deafferentation pain, sympathetically maintained pain, and central pain are subdivisions of these categories.

Neuropathic pain is sometimes called “pathologic” pain because it serves no purpose.⁸¹ A chronic pain state may occur when pathophysiologic changes become independent of the inciting event.⁴⁶ Sensitization plays an important role in this process (see I.B.7-8). Although central sensitization is relatively short lived in the absence of continuing noxious input, nerve injury triggers changes in the CNS that can persist indefinitely.⁴⁸ Thus, central sensitization explains why neuropathic pain is often disproportionate to the stimulus (e.g., hyperalgesia, allodynia) or occurs when no identifiable stimulus exists (e.g., persistent pain, pain spread). Neuropathic pain may be continuous or episodic and is perceived in many ways (e.g., burning, tingling, pricking, shooting, electric shock-like, jabbing, squeezing, deep aching, spasm, or cold).⁹⁷ Table 2 summarizes examples and characteristics of neuropathic pain.

⁸⁸Data from animal studies suggest that the following changes may contribute to neuropathic pain: 1) generation of spontaneous ectopic activity, 2) loss of normal inhibitory mechanisms in the dorsal horn (i.e., central disinhibition), 3) altered primary afferent neuron phenotypes, and 4) sprouting of nerve fibers (i.e., altered neural connections).^{27,63-91-95} Collectively, these changes cause abnormal nerve impulse firing and/or abnormal signal amplification.⁴⁸

C. CLASSIFICATION OF PAIN

Although pain classes are not diagnoses, categorizing pain helps guide treatment. Multiple systems for classifying pain exist. These include multidimensional classification systems, such as the IASP Classification of Chronic Pain,¹⁹ and a variety of systems based on a single dimension of the pain experience. Of the latter systems, those based on pain duration (i.e., acute vs. chronic pain) and underlying pathophysiology (i.e., nociceptive vs. neuropathic pain) are used most often (see I.B.9-10).

This section of the monograph explores the distinction between acute and chronic pain. It also reviews elements of a mixed pain classification system in which pain is categorized as acute pain, cancer pain, or chronic noncancer pain (CNCP).

1. Acute Pain

Acute pain was once defined simply in terms of duration. It is now viewed as a “complex, unpleasant experience with emotional and cognitive, as well as sensory, features that occur in response to tissue trauma.”²² In contrast to chronic pain, relatively high levels of pathology usually accompany acute pain and the pain resolves with healing of the underlying injury. Acute pain is usually nociceptive, but may be neuropathic. Common sources of acute pain include trauma, surgery, labor, medical procedures, and acute disease states. Table 3 summarizes its key features.

Acute pain serves an important biological function, as it warns of the potential for or extent of injury. A host of protective reflexes (e.g., withdrawal of a damaged limb, muscle spasm, autonomic responses) often accompany it. However, the “stress hormone response” prompted by acute injury also can have adverse physiologic and emotional effects (see I.D.3).¹³ Even brief intervals of painful stimulation can induce suffering, neuronal remodeling, and chronic pain;¹⁰ associated behaviors (e.g., bracing, abnormal postures, excessive reclining) may further contribute to the development of chronic pain. Therefore, increasing attention is being focused on the aggressive prevention and treatment of acute pain to reduce complications, including progression to chronic pain states.⁸⁸

Table 2. Examples and Characteristics of Neuropathic Pain

	Painful Mononeuropathies and Polyneuropathies	Deafferentation Pain	Sympathetically Maintained Pain ^a	Central Pain
Definition	Pain along the distribution of one or multiple peripheral nerve(s) caused by damage to the affected nerve(s)	Pain that is due to a loss of afferent input	Pain that is maintained by sympathetic nervous system activity	Pain caused by a primary lesion or dysfunction of the CNS
Pain characteristics and associated symptoms	Three main types: <ul style="list-style-type: none"> • Continuous, deep, burning, aching or bruised pain • Paroxysmal lancinating (shock-like) pain • Abnormal skin sensitivity 	<ul style="list-style-type: none"> • Quality: burning, cramping, crushing, aching, stabbing, or shooting • Hyperalgesia • Hyperpathia • Dysesthesia • Other abnormal sensations 	<ul style="list-style-type: none"> • Quality: burning, throbbing, pressing, or shooting • Allodynia • Hyperalgesia • Associated ANS dysregulation and trophic changes^b 	<ul style="list-style-type: none"> • Quality: burning, numbing, tingling, shooting • Spontaneous and steady or evoked • +/- sensory loss • Allodynia • Hyperalgesia
Sources	<ul style="list-style-type: none"> • Metabolic disorders (e.g., diabetes) • Toxins (e.g., alcohol chemotherapy agents) • Infection (e.g., HIV, herpes zoster) • Trauma • Compressive (nerve entrapment) • Autoimmune and hereditary diseases 	<ul style="list-style-type: none"> • Damage to a peripheral nerve, ganglion, or plexus • CNS disease or injury (occasional) 	<ul style="list-style-type: none"> • Peripheral nerve damage (e.g., CRPS II) • Sympathetic efferent (motor) innervation • Stimulation of nerves by circulating catecholamines 	<ul style="list-style-type: none"> • Ischemia (e.g., stroke) • Tumors • Trauma (e.g., spinal cord injury) • Syring • Demyelination
Clinical examples	<ul style="list-style-type: none"> • Diabetic neuropathy • Alcoholic neuropathy • Postherpetic neuralgia • Carpal tunnel syndrome 	<ul style="list-style-type: none"> • Phantom limb pain • Post-mastectomy pain 	<ul style="list-style-type: none"> • CRPS • Phantom limb pain • Postherpetic neuralgia • Some metabolic neuropathies 	<ul style="list-style-type: none"> • Post-stroke pain • Some cancer pain • Pain associated with multiple sclerosis

Sources: References 22-23, 87, and 97a-97d.

^aSympathetically maintained pain is a pain mechanism, not a diagnosis. It is associated with several types of pain, but it also may exist as a single entity.^{97c}

^bFocal autonomic dysregulation can manifest with signs and symptoms such as swelling, pallor, erythema (redness), sweating, and temperature changes. Trophic changes include thinning of the skin, abnormal hair or nail growth, and bone changes.

ANS: autonomic nervous system; CNS: central nervous system; CRPS: complex regional pain syndrome types I and II; CRPS II: complex regional pain syndrome type II; HIV: human immunodeficiency virus.

2. Chronic Pain

Chronic pain was once defined as pain that extends 3 or 6 months beyond onset or beyond the expected period of healing.⁹⁸ However, new definitions differentiate chronic pain from acute pain based on more than just time (Table 3). Chronic pain is now recognized as pain that extends beyond the period of healing, with levels of identified pathology that often are low and insufficient to explain the presence and/or extent of the pain.⁹⁹ Chronic pain is also defined as a persistent pain that “disrupts sleep and normal living, ceases to serve a protective function, and instead degrades health and functional capability.”¹⁰¹ Thus, unlike acute pain, chronic pain serves no adaptive purpose.

Chronic pain may be nociceptive, neuropathic, or both and caused by injury (e.g., trauma, surgery), malignant conditions, or a variety of

chronic non-life-threatening conditions (e.g., arthritis, fibromyalgia, neuropathy). In some cases, chronic pain exists de novo with no apparent cause. Although injury often initiates chronic pain, factors pathogenetically and physically remote from its cause may perpetuate it.⁹⁸ Environmental and affective factors also can exacerbate and perpetuate chronic pain, leading to disability and maladaptive behavior.

3. Cancer Pain

Pain associated with potentially life-threatening conditions such as cancer is often called “malignant pain” or “cancer pain.” However, there is movement toward the use of new terms such as “pain associated with human immunodeficiency virus (HIV) infection” or “pain associat-

Table 3. Key Features of Pain Types and Syndromes

Type of Pain	Features
Acute pain	Pain usually concordant with degree of tissue damage, which remits with resolution of the injury Reflects activation of nociceptors and/or sensitized central neurons Often associated with ANS and other protective reflex responses (e.g., muscle spasm, “splinting”)
Chronic pain	Low levels of identified underlying pathology that do not explain the presence and/or extent of the pain Perpetuated by factors remote from the cause Continuous or intermittent with or without acute exacerbations Symptoms of ANS hyperactivity less common Irritability, social withdrawal, depressed mood and vegetative symptoms (e.g., changes in sleep, appetite, libido), disruption of work, and social relationships
Cancer pain	Strong relationship between tissue pathology and levels of pain Limited time frame that permits aggressive pain management Rarely involves medical-legal or disability issues
CNCP	Weak relationship between tissue pathology and pain levels Prolonged, potentially life-long, pain May involve medical, legal, disability issues/conflicts, work or relationship problems, physical deconditioning, psychological symptoms (see chronic pain above) May progress to CPS
CPS	Preoccupation with somatic functioning Lifestyle centered on seeking immediate pain relief, with excessive, nonproductive, and often harmful use of health care services Repeated attempts to obtain pain-related financial compensation (e.g., Social Security, Veterans’ benefits) Numerous symptoms and signs of psychosocial dysfunction that the patient attributes to the pain (e.g., anger, depression, anxiety, substance abuse, disrupted work or personal relationships)

Sources: References 88 and 98-100.
ANS: autonomic nervous system; CNCP: chronic noncancer pain; CPS: chronic pain syndrome; VA: Veterans Administration.

ed with cancer.” (The term “cancer pain” is used in this monograph for the sake of brevity.)

Cancer pain includes pain caused by the disease itself (e.g., tumor invasion of tissue, compression or infiltration of nerves or blood vessels, organ obstruction, infection, inflammation) and/or painful diagnostic procedures or treatments (e.g., biopsy, postoperative pain, toxicities from chemotherapy or radiation treatment).¹⁰²

There are several reasons why some experts feel that cancer pain merits a discrete category. First, its acute and chronic components and multiple etiologies make it difficult to classify based on duration or pathology alone. Second, cancer pain differs from chronic noncancer pain (CNCP) in some significant ways (e.g., time frame, levels of pathology, treatment strategies) (Table 3).⁹⁹ However, there is little evidence to support a distinction between these pain types based on underlying neural processes. Therefore, many pain experts categorize cancer pain as acute or chronic pain.⁹⁸

4. Chronic Noncancer Pain

A subtype of chronic pain is CNCP, which refers to persistent pain not associated with cancer. In contrast to patients with chronic cancer pain, patients with CNCP often report pain lev-

els that only weakly correspond to identifiable levels of tissue pathology and/or respond poorly to standard treatments.⁹⁹⁻¹⁰⁰ As CNCP may last for many years, some consider use of the traditional term for such pain, “chronic nonmalignant pain,” inappropriate. Thus, there is movement toward use of alternate terms such as “chronic noncancer pain” and “chronic non-cancer-related pain.”

Causes of CNCP include acute injury that has proceeded to chronic pain (e.g., whiplash) and various chronic conditions (Table 4). In some cases, there is no discernable cause, and the pain is considered the disease. CNCP can affect virtually any body system or region, and pain severity ranges from mild to excruciating. Some types of CNCP have well-defined characteristics and patterns, whereas others do not. Neuropathic and myofascial CNCP can be particularly hard to diagnose, as they may occur in the absence of a known injury or disease process.¹⁰⁰

Because of its chronicity and impact on daily activities, patients with CNCP may experience vocational, interpersonal, and/or psychological problems (Table 3).¹⁵ If the symptoms of CNCP consume the attention of and incapacitate the patient, he or she may suffer from a psychosocial disorder known as “chronic pain syndrome” (CPS) (Table 3).¹⁰⁰ The pain experienced by these patients is real, and not all patients with CNCP develop this syndrome. Appropriate man-

Table 4. Examples of Chronic Noncancer Pain

- Osteoarthritis
- Low back pain
- Myofascial pain
- Fibromyalgia
- Headaches (e.g., migraine^a, tension-type, cluster)
- “Central pain” (e.g., spinal cord injury, stroke, MS)
- Chronic abdominal pain (e.g., chronic pancreatitis, chronic PUD, IBS)
- Sickle cell disease^a
- CRPS, Types I and II
- Phantom limb pain
- Peripheral neuropathy
- Neuralgia (e.g., post-herpetic, trigeminal)

Sources: References 99 and 100.

^aMigraines and sickle cell disease may be more accurately classified as intermittent pain but are treated as chronic noncancer pain for purposes of this discussion.

CRPS: complex regional pain syndrome; IBS: Irritable bowel syndrome; MS: multiple sclerosis; PUD: peptic ulcer.

agement of both CNCP and CPS requires an interdisciplinary approach that addresses the complex interaction of physical, psychological, and social factors that contribute to the ongoing pain.

D. PREVALENCE, CONSEQUENCES, AND COSTS OF PAIN

Pain is common, and inadequately managed pain is associated with many adverse consequences. This section of the monograph reviews epidemiological data, evidence that pain is undertreated, and consequences of inadequately managed pain. These consequences affect patients, their families, and society as a whole and can be broadly categorized as physiological, psychosocial (quality of life), and financial.

1. What Is the Size and Scope of Pain As A Health Care Problem?

Acute pain is the most common reason why patients seek medical attention.⁸⁸ Common reasons for visits to health care professionals include acute pain (e.g., musculoskeletal pain,

gastrointestinal pain, chest pain, headache) and injuries (e.g., fractures, sprains, lacerations).¹⁰³ Chronic pain is also a problem of epidemic proportions. About 50 million of the estimated 75 million Americans who live with “serious pain” suffer from chronic pain.¹⁰⁴ Many have been living with their pain for more than 5 years and experience pain almost 6 days a week.¹⁴ A survey of self-help organization members suggested that back and neck pain, myofascial pain/fibromyalgia, headache, arthritis pain, and neuropathic pain are the most common types of CNCP.¹⁰⁵ Low back pain, arthritis, and migraine headache alone account for pain in tens of millions of Americans.⁸⁸

2. What Evidence Suggests That Pain Is Undertreated?

In 1992, the AHCPR developed a CPG for acute pain management, in part due to mounting reports of inadequate postoperative pain control.¹³ Clinical surveys indicated that routine orders for as-needed intramuscular (IM) injections of opioids failed to relieve pain in about half of all postoperative patients (e.g., Marks and Sachar,¹⁰⁶ Donovan et al.,¹⁰⁷ Oden¹⁰⁸). This finding prompted recommendations including the scheduled administration of pain medications via other routes. A national survey of perioperative pain in hospitalized patients recently assessed adherence to these and other (American Society of Anesthesiologists) CPGs.¹⁰⁹ Although overall guideline adherence was excellent, frequent IM administration of opioids and infrequent use of nonpharmacologic pain management methods were important exceptions.

Results of other 1990s studies (e.g., Abbott et al.,¹¹⁰ Gu and Belgrade,¹¹¹ Ward and Gordon,¹¹² Warfield and Kahn,¹¹³ Drayer et al.¹¹⁴) contribute to concerns about the management of acute pain. In one study of pain management in hospitalized patients, 61% of the 217 patients interviewed reported pain ratings of 7 to 10 (on a scale from 0 for no pain and 10 for the worst imaginable pain) within the preceding 24 hours.¹¹² Forty-nine percent reported a current pain level between 4 and 10, and this was after analgesic administration in 20%. A study of the adequacy of analgesia in an urban emergency department produced some disturbing results. Hispanic patients with long-bone fractures were half as likely as non-Hispanic white patients to receive pain medication.¹¹⁵

A 1998 survey of a random cross-section of

U.S. households suggests that CNCP also is undertreated.¹⁴ Of 805 adults interviewed, 70% reported sufficient control of moderate pain. However, this percentage decreased to 51% in patients with severe pain and to 39% in those with very severe pain. Results from a 2001 survey suggest that most individuals with severe CNCP still do not have their pain under control.¹⁴ Of those who do, it took almost half of them a year to achieve adequate pain control.¹⁴

Undertreatment of cancer pain also is well documented. A landmark study involved 1308 cancer outpatients at 54 treatment sites.¹¹⁶ Approximately two-thirds (67%) of the patients interviewed reported pain sufficient to require daily analgesics, and 36% reported that the pain limited their ability to function. However, only 42% of those with pain reported receiving sufficient pain relief. Data from more recent studies (e.g., Zhukovsky et al.,¹¹⁷ Cleeland et al.,¹¹⁸ Anderson et al.,¹¹⁹ Wolf et al.,¹²⁰ Weiss et al.¹²¹) suggest that pain associated with terminal illnesses, including cancer, is still undertreated. Elderly, female, minority, and pediatric patients are at greatest risk for inadequate management of cancer pain.^{120,122}

3. What Are the Consequences and Costs of Undertreatment of Pain?

a. *Physiological consequences*

As discussed in Section I.C.1, acute tissue injury triggers physiological “stress” responses intended to protect the body. Yet these responses can have adverse effects if allowed to persist unchecked. Table 5 summarizes some of the adverse physiological consequences of inadequately controlled postinjury and postoperative pain (e.g., pneumonia, blood clots, infection, shock). Very young, very old, and frail patients are at greatest risk for such complications.¹³ In one study of neonates who underwent cardiac surgery, patients who received “light” versus “deep” anesthesia and postoperative analgesia had higher mortality rates.¹²³

Another key adverse effect of poorly controlled acute pain is progression to chronic pain.¹²⁴⁻¹²⁵ Some chronic neuropathic pain (e.g., postmastectomy pain, postthoracotomy pain, phantom limb pain) results, in part, from a lack of aggressive pain management and/or early rehabilitation following surgery.¹²⁶⁻¹²⁷ Inadequate control of pain associated with acute herpes zoster (shingles) may increase the likelihood of subsequent postherpetic neuralgia.¹²⁸

Table 5. Examples of Physiological Consequences of Unrelieved Pain

Functional Domain	Stress Responses to Pain	Examples of Clinical Manifestations
Endocrine/metabolic	Altered release of multiple hormones (e.g., ACTH, cortisol, catecholamines, insulin) with associated metabolic disturbances	Weight loss Fever Increased respiratory and heart rate Shock
Cardiovascular	Increased heart rate Increased vascular resistance Increased blood pressure Increased myocardial oxygen demand Hypercoagulation	Unstable angina (chest pain) Myocardial infarction (heart attack) Deep vein thrombosis (blood clot)
Respiratory	Decreased air flow due to involuntary (reflex muscle spasm) and voluntary (“splinting”) mechanisms that limit respiratory effort	Atelectasis Pneumonia
Gastrointestinal	Decreased rate of gastric emptying Decreased intestinal motility	Delayed gastric emptying, constipation, anorexia, ileus ^a
Musculoskeletal	Muscle spasm Impaired muscle mobility and function	Immobility Weakness Fatigue
Immune	Impaired immune function	Infection
Genitourinary	Abnormal release of hormones that affect urine output, fluid volume, and electrolyte balance	Decreased urine output Hypertension (fluid retention) Electrolyte disturbances

Sources: References 13 and 23.

^aMechanical, dynamic, or adynamic obstruction of bowel often manifests as colicky pain, distension, vomiting, and absence of the passage of stool.

ACTH: adrenocorticotropic hormone.

One study showed that pain levels in patients hospitalized for serious conditions (e.g., chronic obstructive pulmonary disease, liver failure, cancer) determined future pain levels.¹²⁹ Undertreated pain early in life is associated with pain later in life.¹³⁰⁻¹³¹

b. *Quality of life*

Inadequate control of pain interferes with the pain sufferer's ability to carry out activities of daily living (e.g., work, relationships, hobbies, sex).¹⁴ It also has adverse psychological consequences. Patients with inadequately managed pain may experience anxiety, fear, anger, depression, or cognitive dysfunction,¹⁵ and family members report varying levels of helplessness, frustration, and "heartbreak."¹³²

These consequences are especially likely to occur in patients with chronic pain. These individuals report impairments on multiple measures of physical, social, and psychological well-being, and many experience psychological symptoms (e.g., depression, anxiety) that adversely influence health care.¹⁵ Left unchecked, these symptoms can contribute to more serious consequences. In one study, about half of the patients with CNCP reported that they had considered suicide despite the availability of resources and coping strategies.¹⁰⁵

c. *Financial consequences*

Pain costs Americans an estimated \$100 billion each year.^{4,133} Patients, families, health care organizations, and society bear this financial burden. Patients with chronic pain are five times as likely as those without chronic pain to use health care services.¹⁵ In addition, medical complications associated with inadequately controlled acute pain can increase length of stay, rehospitalization rates, and outpatient visits.¹³⁵ Results from some studies (e.g., Burke et al.^{h,135}) suggest that adequate management of acute (postoperative) pain can reduce length of stay and costs.

Pain is also costly in terms of lost productivity and income. It is a leading cause of medically related work absenteeism and results in more than 50 million lost work days per year in the United States.^{2,136} About 25% of the population in industrialized nations suffers from chronic pain of sufficient severity that they miss days of

work.¹³⁷ Individuals with chronic pain often face long-term or permanent unemployment or underemployment.

E. BARRIERS TO THE APPROPRIATE ASSESSMENT AND MANAGEMENT OF PAIN

The undertreatment of pain reflects barriers to both assessment and management. These barriers can be broadly categorized as those attributable to the health care system, clinicians, patients and families, laws and regulations, and society.^{134,138-139} Collectively, these barriers contribute to a failure to assess pain, to accept the patient's self-report of pain, and/or to take appropriate action.¹⁴⁰

1. Barriers Within the Health Care System

Systems barriers to pain assessment and management include an absence of clearly articulated practice standards and failure of the system to make pain relief a priority.^{134,141-142} For example, some health care organizations fail to adopt a standard pain assessment tool or to provide staff with sufficient time and/or chart space for documenting pain-related information.¹³⁴ Others fail to provide clinicians with practical tools and training to improve pain management such as CPGs, algorithms, protocols, and computer help screens. However, the greatest systems barrier to appropriate pain management is a lack of accountability for pain management practices. Institutions and health care organizations must implement means of holding clinicians accountable for adequate pain assessment and management (e.g., chart audits of pain documentation, pain competencies in staff orientation and performance evaluations, formal reviews for critical incidents) to ensure effective pain management.¹³⁴

Recent changes in the health care system (e.g., growth of managed care, shift from inpatient to outpatient treatment settings, new reimbursement policies) also have introduced barriers

^hBurke et al. compared resource utilization and costs between groups of patients who did or did not receive ketorolac for management of postoperative pain.¹³⁵

to pain management. Patient care is more fragmented; thus, the risk of poor coordination of care across treatment settings is increased.^{141,143} The use of gatekeepers and formularies by managed care organizations may impede access to pain specialists, comprehensive pain management facilities, and certain analgesic therapies.^{141,143} In addition, inconsistent reimbursement policies for pain treatment, or concern that aggressive treatment will increase costs, can lead to inadequate treatment of pain.¹⁴⁴

2. Health Care Professional Barriers

Clinicians' attitudes, beliefs, and behaviors contribute to the undertreatment of pain. For example, some clinicians do not view pain relief as important and/or do not want to "waste time" assessing pain.¹⁴¹ Others refuse to accept that the patient's self-report is the most reliable indicator of pain. Studies have shown that lack of assessment, underassessment, and a disparity between the clinician's and the patient's ratings of pain intensity are major causes of inadequately controlled pain (e.g., Donovan et al.,¹⁰⁷ Drayer et al.,¹¹⁴ Grossman et al.,¹⁴⁵ Gu and Belgrade,¹¹¹ Paice et al.,¹⁴⁶ Von Roenn et al.¹⁴⁷). Inappropriate or exaggerated concerns and inadequate or inaccurate clinical knowledge also limit clinicians' abilities to appropriately manage pain.^{139,141,144} Concerns often relate to aspects of pharmacologic treatment such as regulatory scrutiny, analgesic side effects, and iatrogenic addiction (see I.E.5). Problems with clinical knowledge include inadequate understanding of pharmacology and misconceptions about pain (Table 6).

3. Patient and Family Barriers

Whereas poor clinician-patient communication may reflect deficits in the clinician's skills, certain patient characteristics (e.g., age, language, cognitive abilities, coexisting physical or psychological illness, cultural traditions) may impair a patient's ability to communicate.¹³ Alternatively, patients may be reluctant to report pain to clinicians due to low expectations of obtaining relief, stoicism, fears, or concerns about what the pain means (e.g., worsening disease, death), analgesic side effects, or addiction.¹⁴¹ In a recent survey of terminally ill patients, whereas half experienced moderate to

severe pain, only 30% wanted additional pain treatment.¹²¹ Reasons the patients offered for declining additional therapy included fear of addiction, dislike of mental or physical drug side effects, and not wanting to take more pills or injections.

Other patient and family factors that contribute to the undertreatment of pain include financial barriers (e.g., lack of health insurance, high cost of certain medications) and even poor adherence to treatment regimens.^{14,141} Limited data suggest that patients do not always take analgesics as prescribed.¹⁴⁸⁻¹⁵⁰ In addition, some patients with chronic pain do not seek medical attention. A recent survey of individuals with CNCP suggested that, while most chronic pain sufferers have visited a doctor at some point, almost 40% are not currently under the care of a physician.¹⁴ Difficulty in locating a clinician who could effectively manage their pain was a commonly cited reason.

Table 6. Common Misconceptions About Pain

The incorrect beliefs that:

- Physical or behavioral signs of pain (e.g., abnormal vital signs, grimacing, limping) are more reliable indicators of pain than patient self-report.
- Elderly or cognitively impaired patients cannot use pain intensity rating scales.
- Pain does not exist in the absence of physical or behavioral signs or detectable tissue damage.
- Pain without an obvious physical cause, or that is more severe than expected based on findings, is usually psychogenic.
- Comparable stimuli produce the same level of pain in all individuals (i.e., a uniform pain threshold exists).
- Prior experience with pain teaches a person to be more tolerant of pain.
- Analgesics should be withheld until the cause of the pain is established.
- Noncancer pain is not as severe as cancer pain.
- Patients who are knowledgeable about pain medications, are frequent emergency department patrons, or have been taking opioids for a long time are necessarily addicts or "drug seekers."
- Use of opioids in patients with pain will cause them to become addicted.
- Patients who respond to a placebo drug are malingering.
- Neonates, infants, and young children have decreased pain sensation.

Sources: References 13 and 140.

4. Legal and Societal Barriers

Legal and societal issues also contribute to the undertreatment of pain. The former include restrictive laws or regulations about the prescribing of controlled substances as well as confusion about the appropriate role of opioids in pain treatment.^{141,151} Societal issues that contribute to the undertreatment of pain include drug abuse programs and erroneous beliefs about tolerance, physical dependence, and addiction (see I.E.5). For example, some clinicians incorrectly assume that exposure to an addictive drug usually results in addiction.

5. Tolerance, Physical Dependence, and Addiction

a. Definitions

Many medications, including opioids, play important roles in pain management. However, concerns about their potential misuse and misunderstanding of the nature and risk of addiction limit their appropriate use.¹⁵² Disparate definitions of tolerance, physical dependence, and addiction contribute to this problem. Therefore, the American Society of Addiction Medicine (ASAM), the American Academy of Pain Medicine (AAPM), and the American Pain Society (APS) recently recommended use of the following definitions:¹⁵²

- **Tolerance:** “Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug’s effects over time.”
- **Physical Dependence:** “Physical dependence is a 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 level of the drug, and/or administration of an antagonist.”
- **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.”

Although other definitions exist (e.g., DSM-IV), experts consider these terms the most applicable to pain management. A related term,

pseudoaddiction, refers to patient behaviors that may occur when pain is undertreated, including increased focus on obtaining medications (“drug seeking”), “clock watching,” and even illicit drug use or deception.¹⁵³ Pseudoaddiction can be distinguished from true addiction because such behaviors resolve with effective pain management.¹⁵²

b. Etiology, issues, and concerns

Many medications produce tolerance and physical dependence, and some (e.g., opioids, sedatives, stimulants, anxiolytics, some muscle relaxants) may cause addiction in vulnerable individuals.¹⁵² Most experts agree that patients who undergo prolonged opioid therapy usually develop physical dependence but do not develop addictive disorders.¹⁵² In general, patients in pain do not become addicted to opioids. Although the actual risk of addiction is unknown,¹⁵² it is thought to be quite low. A recent study of opioid analgesic use revealed “low and stable” abuse of opioids between 1990 and 1996 despite significant increases in opioids prescribed.¹⁵⁴ Drug exposure appears to be only one etiologic factor in the development of addiction,¹⁵² and genetic, social, and psychological factors may be more significant determinants.¹⁵⁵⁻¹⁵⁸

Fear of causing addiction (i.e., iatrogenic addiction), particularly with opioid use, is a major barrier to appropriate pain management.^{8,159-162} This fear sometimes reflects a lack of understanding of the risk of addiction with therapeutic drug use. Although studies suggest that the risk of iatrogenic addiction is quite low (e.g., Perry and Heidrich,¹⁶³ Zenz et al.¹⁶⁴), surveys indicate that clinicians often overestimate this risk.¹⁶⁵⁻¹⁶⁷ Alternatively, clinicians may be reluctant to prescribe an opioid because they have witnessed the devastation that addiction can cause in a patient’s life.

Clinicians are also often reluctant to prescribe opioids due to concerns about licensing issues, peer review, state disciplinary action, and even legal prosecution (i.e., for over-prescribing, or under-prescribing, controlled substances).¹⁰⁴ The Federation of State Medical Boards of the United States (FSMB) acknowledges such potential in their 1998 “Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.”¹⁶⁰ These guidelines attribute inadequate pain control to three major factors:

- Physicians’ lack of knowledge about pain management,
- Inadequate understanding of addiction, and

- Fear of investigation or sanction by federal, state, and local regulatory agencies.¹⁶⁰

These guidelines acknowledge that: “controlled substances, including opioid analgesics, may be essential in the treatment of acute pain due to trauma or surgery and chronic pain, whether due to cancer or non-cancer origins.”¹⁶⁰ They assert that physicians should not fear disciplinary action for prescribing, dispensing, or administering controlled substances for a legitimate medical purpose (including pain) in the usual course of professional practice.¹⁶⁰ However,

they also state that “all such prescribing must be based on clear documentation of unrelieved pain and in compliance with applicable state or federal law.”¹⁶⁰ These guidelines and other information about regulatory issues are located at www.fsmb.org/policy.htm and <http://www.medsch.wisc.edu/painpolicy>, respectively, on the World Wide Web. The latter URL also contains up-to-date information on specific state laws and regulations.