LAYOUT

JOB#: Module 1: Glossary callouts

Circulation Round
0 2 3 4 5 6 7 8 9 10

Team Review:

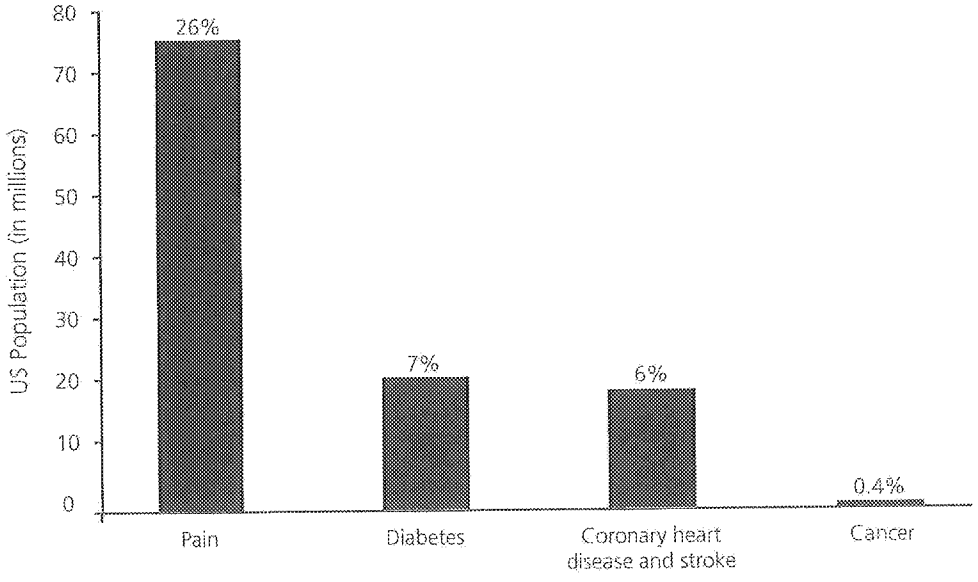
	Initial	Date
Executive Team:		
Creative:	KS	8/23
Medical:	KL	8/23 2:45 pm
Client Services:		
Project Management:	JM	8/23
Event Planning:		
Operations:		

najor components: persistent pain
ersistent pain is chronic pain that lasts
; to a transient exacerbation of pain
ise stable, baseline persistent pain.[6]
e persistent pain treated with around-
[5] BTP can be severe in intensity, with
short duration. It occurs because of
pain, for idiopathic reasons, or during
ATC medications.[6, 7] Therefore, the 3
ain; (2) idiopathic pain; and (3) end-
ly impact a patient's quality of life and
; to provide adequate pain medications
d.

close up and delete hyphen

port experiencing pain that has persisted
dividuals than those with a diagnosis
er combined (Figure 1).[8] Estimates of
t commonly defined as pain lasting for
%.[9, 10, 11, 12] Some of the most common
States include joint pain, low back pain,
migraine.[13]

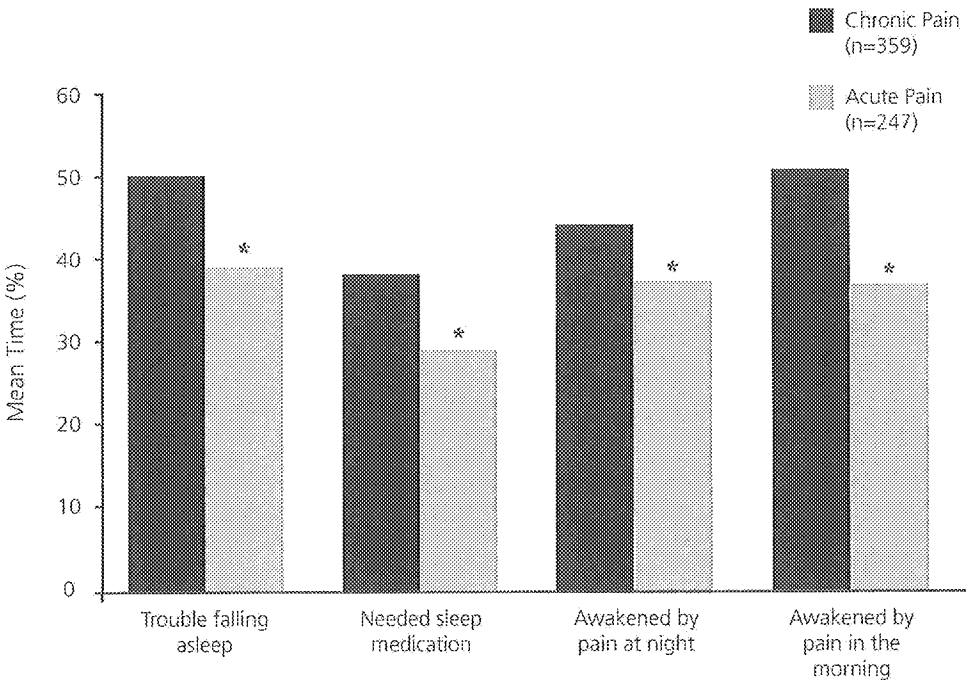
ain, Diabetes, Heart Disease,
and Cancer in the United States



Source: American Pain Foundation Web site. http://www.painfoundation.org.[8]

Notes:

Figure 3. Impact of Pain on Sleep



*$P<0.05$ between chronic and acute pain groups.
Source: McCarberg BH et al. *Am J Ther.* 2008;15:312-320.[14]

Chronic pain exerts negative effects on employment status and work productivity.[14] Approximately one-third of patients with chronic pain report that they are worried about losing their job because of their pain disorder. Patients report losing an average of 19.2 workdays per year because of chronic pain.[14] Among workers actively engaged in work, chronic pain associated with headache, arthritis, back problems, and other musculoskeletal conditions costs up to $60 billion per year in lost productivity.[15]

Neurobiology of Pain

Pain Pathways and Mechanisms

Nociception is the process by which noxious sensory stimuli are transmitted from the periphery to the central ne sory information acquired from the envi uraxis levels and then relayed to the neoc ior cingulate cortex—2 major cortical c s.[16]

noxious sensory stimuli—Thermal, mechanical, or chemical stimuli that interact with the nerve terminals in the peripheral nervous system to illicit a pain response.

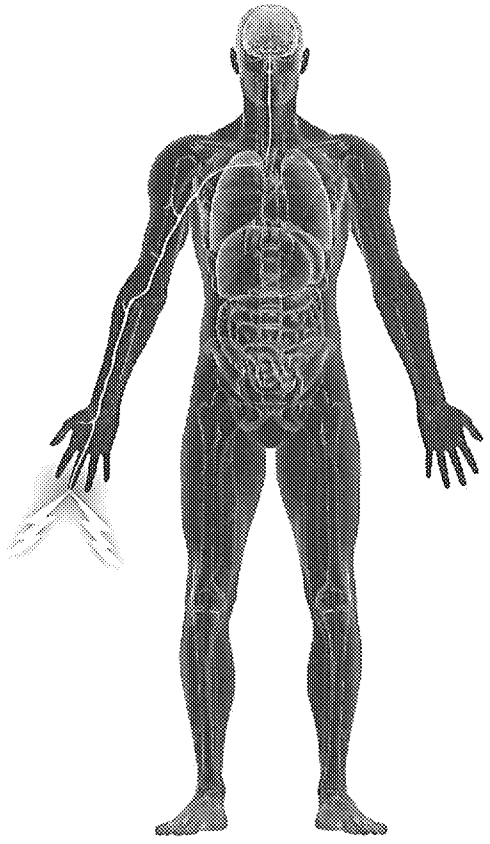
Notes:

Notes:

Nociception is described as occurring in 4 or 5 stages (many descriptions combine the transmission and conduction stages) (Figure 5).[17] During transduction, energy from a noxious thermal, mechanical, or chemical action potentials by primary afferent iceptive elements express numerous t modulate their mechanical, thermal, ble, tissue damage results in the release of a number of chemical and protein mediators from ruptured cells. Prostaglandins, histamine, serotonin, cytokines, adenosine triphosphate (ATP), hydrogen ions, and bradykinin, among others, either activate nociceptors to generate efferent nerve impulses or sensitize nociceptors beyond their normal resting state by lowering activation thresholds and thus increasing their excitability.[17] For a more complete description of this process, see *Module 2*.

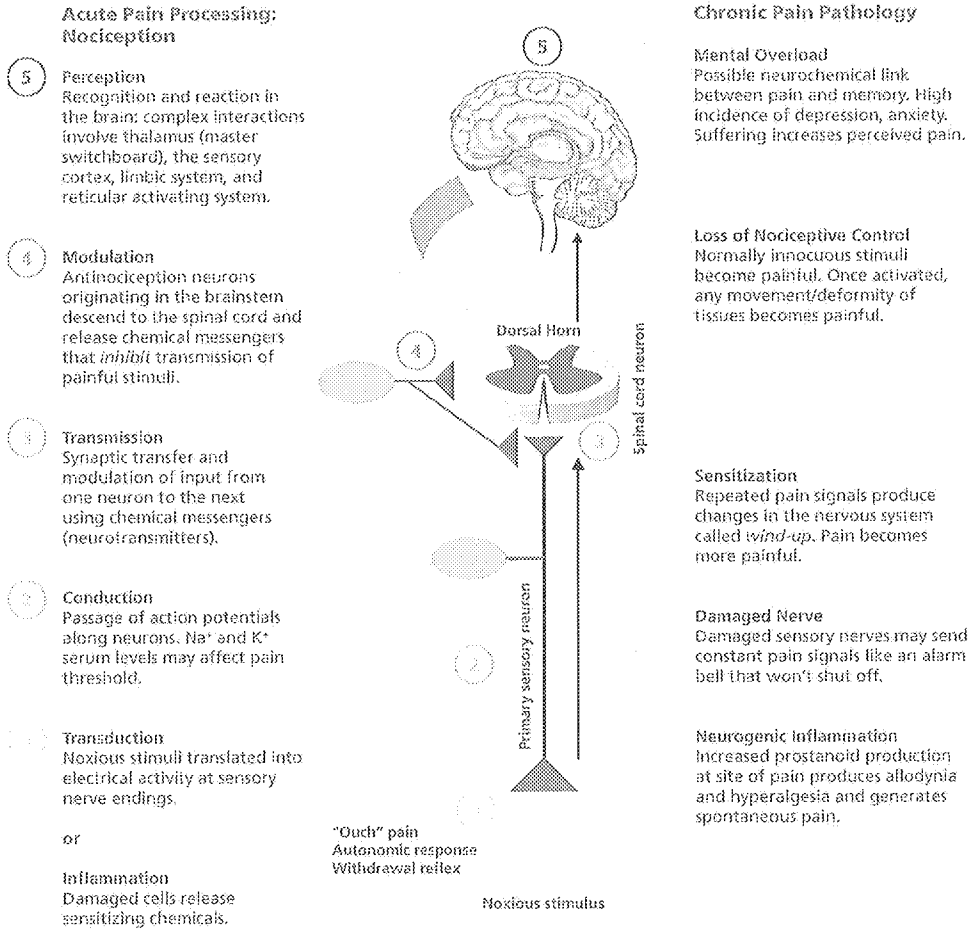
transduction—The process by which painful stimuli are transformed into nerve impulses. ✓

Figure 4. Transmission of Noxious Stimulus From the Periphery to the Central Nervous System (Nociception)



need printout for nociceptors (also on this page) ✓ AW
[see edits on glossary]

Figure 5: Comparison Between Acute and Chronic Pain Processes



Source: Whitten CE et al. *Permanente J.* 2005;9:10.[17]

Neural transmission is the process by which nerve signals generated in the pe[illegible]nd brain (Figure 6).[17, 18] This involve[illegible]d synaptic modulation between neuron[illegible]rotransmitters). Nociceptors transm[illegible]ng either unmyelinated C-fiber or thin[illegible]e primary afferent neurons transfer the nociceptive signals to dorsal horn neurons at synapses mediated by excitatory neurotransmitters.[2, 19] The dorsal horn also includes spinal interneurons, which release inhibitory neurotransmitters and endogenous opioids to blunt local nociceptive transmission both presynaptically and postsynaptically.[2] From the dorsal horn, signals are then relayed along central ascending tracts to the thalamus, hypothalamus, mesencephalon, reticular formation, and cerebral cortex.[2] See *Module 2* for a more complete review of the neuropharmacology.

transmission—The process by which nerve impulses from the site of injury are transmitted to the spinal cord and brain.

Notes:

Nociceptive Pain

wrong definition

Nociceptive pain refers to the transient responses of nociceptors to noxious

neuropathic pain—Pain resulting from damage to the nervous system that interferes with normal pain signal processing. Neuropathic pain is perceived in various ways, including tingling, numbness, stabbing, and shooting sensations.

eptive pain may become
s recurrent or ongoing noxious
steoarthritis).[23] Nociceptive pain is
ntaneous pain and hypersensitivity
n.[2] Tissue injury and inflammation
ociceptive terminals as damaged
cells release their contents and inflammatory cells are recruited to the site of injury to produce cytokines, chemokines, and growth factors.[2] The effluent of damaged

cytokine—Generic term for proteins that act as mediators in immune response via G-protein–coupled receptors. Some cytokines associated with pain include interleukins and tumor necrosis factor. ✓

ectly
activate the nocicep
becomes
hypersensitive to fut
utor
to the inflammatory
nes
associated with infla
reduces
pain thresholds and increases the responsiveness of peripheral nociceptors.[24]

Nociceptive pain can be further categorized as somatic (rooted in the skin or deep tissues)

somatic pain—Pain resulting from activation of nociceptors in the cutaneous (skin) or deep tissues (muscles, tendons, bones). Somatic pain is typically dull or aching but well localized. ✓

Common examples of
somatic pain
matoid arthritis (RA),
and low back
onic pancreatitis.[26]
Visceral pain
n nociceptive pain and
innervation o
sparsely innervated
relative to sor
f a given visceral
element may arise in several spinal segments and can involve both ipsilateral and contralateral spinal divisions.[30] This more diffuse innervation may explain the difficulty in localizing visceral pain, as well as the relative insensitivity of visceral tissue to focal tissue damage.[28] Spinal neurons that receive visceral afferents also receive convergent input from cutaneous or deeper structures, resulting in referred pain.[29, 31] Somatic structures generally conduct noxious stimuli through Aδ fibers and C fibers, whereas the viscera must encode both innocuous and noxious stimuli through Aδ fibers and C fibers.[28]

Notes:

Continued inappropriate discharge by damaged nerves can trigger central sensitization—activity-dependent plasticity in the central nervous odynia and hyperalgesia.[24] Central sensitization pain[24] and can be driven and maintained via ntact afferent neurons.[41]

central sensitization—Increased sensitivity of spinal neurons due to persistent or large-scale release of glutamate can overload NMDA (N-methyl-D-aspartate) receptors that result long-term sensitization.

ed and maintained when low-threshold diate nonpainful sensations, transmit pain-heral nerve injury.[23, 42] Apoptosis of primary ons after peripheral nerve injury and subsequent reorganization of sensory pathways may also play a significant role.[23, 43, 44] Disinhibition modulating spinal transmission of nociceptive input may lead to the promotion of Aβ fiber-mediated pain.[23] A variety of mechanisms may also contribute to loss of pre- and postsynaptic GABAergic inhibition of the spinal cord.[23]

GABAergic—GABA (γ-aminobutyric acid) is a neurotransmitter located in both pre- and postsynaptic neurons and is responsible for the conduction of several synaptic signals. In pain, it is an inhibitory neurotransmitter in the descending bulbospinal inhibitory interneurons located in the central nervous system.

Functional Pain

Functional pain —induced allodynia and hyp gic deficits or peripheral abnorm fibromyalgia, although it can be vel syndrome.[2] In some cases, amplification of responses is not limited to pain stimuli, suggesting widespread increases in the sensitivity of sensory systems.[2] Examples of functional pain include[2]:

- Fibromyalgia
- Irritable bowel syndrome
- Noncardiac chest pain
- Tension-type headache

Assessment of Chronic Pain

Reliable assessment of pain levels and functional consequences is important for both clinical trials and effective pain management in clinical practice.[45] In both settings, it is essential to measure the patient's baseline pain and how the pain changes over time in response to treatment, disease changes, and other variables. Without assessment and reassessment, it is exceedingly difficult to determine if the patient is experiencing adequate analgesia.

Notes:

Continued inappropriate discharge by damaged nerves can trigger central sensitization—activity-dependent plasticity in the central nervous system that can manifest as allodynia and hyperalgesia.[24] Central sensitization can contribute to neuropathic pain[24] and can be driven and maintained via peripheral sensitization of intact afferent neurons.[41]

Neuropathic pain may be elicited and maintained when low-threshold Aβ fibers, which normally mediate nonpainful sensations, transmit pain-related signals following peripheral nerve injury.[23, 42] Apoptosis of primary sensory and dorsal horn neurons after peripheral nerve injury and subsequent reorganization of sensory pathways may also play a significant role.[23, 43, 44] Disinhibition modulating spinal transmission of nociceptive input may lead to mediated pain.[23] A variety of mechanisms may and postsynaptic GABAergic inhibition of the

disinhibition—Reduction of synaptic inhibition

Temporary loss of nerve transmission inhibition due to drug or disease.

Functional Pain

Functional pain refers to states in which central sensitization—induced allodynia and hyperalgesia—occurs in the absence of neurologic deficits or peripheral abnormalities.[2] Often the pain is widespread, as in fibromyalgia, although it can be more localized as observed in irritable bowel syndrome.[2] In some cases, amplification of responses is not limited to pain stimuli, suggesting widespread increases in the sensitivity of sensory systems.[2] Examples of functional pain include[2]:

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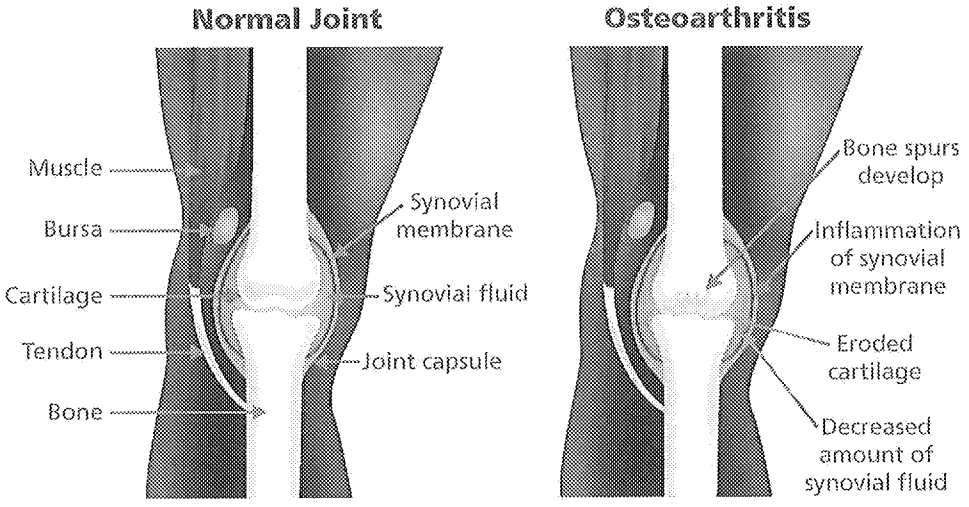
Notes:

Figure 12. Primary Osteoarthritis of the Knee



Source: Mayo Foundation for Education and Research.

Lifestyle modification (such as weight loss and exercise), physical therapy, and over-the-counter analgesics are treatment mainstays.[70] According to the ACR Guidelines, acetaminophen is the recommended initial pharmacologic approach, with oral nonsteroidal anti-inflammatory drug (NSAID) therapy recommended if pain relief with acetaminophen is insufficient.[70] Topical NSAIDs may be recommended as an alternative to oral therapy, particularly in patients at high risk for NSAID-related gastrointestinal or cardiovascular serious adverse events. Tramadol and opioid treatment are recommended for patients with moderate to severe pain in whom NSAIDs are contraindicated or for whom previous oral therapy was inadequate.[70]

Glucosamine/chondroitin complex supplements and hyaluronic acid injections have shown efficacy in some patients.[75, 76] Ultimately, if pain becomes debilitating, elective joint replacement surgery may be recommended.[70] For a detailed overview of treatment practices and guidelines for OA, see Module 6 in the PENNSAID Advanced Training Series.

Insights and Implications

Although they are generally well tolerated when prescribed and used appropriately, acetaminophen, oral NSAIDs, and opioid analgesics are associated with serious risks. It is therefore important for healthcare professionals to properly assess patients prior to initiating therapy and to take appropriate measures to ensure the benefit of therapy outweighs the potential risk (see *Modules 5 and 6* for discussion of risk management strategies). Topical NSAIDs have shown benefit in pain relief for OA, with lower systemic concentrations, and are theoretically associated with reduced risk of serious

Notes:

Peripheral Neuropathy

Etiology, Clinical Presentation, and Epidemiology

Chronic neuropathic pain arises from a diverse class of neuropathologies characterized by physical damage to the nervous system and surrounding/supporting structures.[107] Commonly encountered neuropathic pain states include[2, 32, 33]:

- Nerve compression
- Multiple sclerosis
- HIV/AIDS
- Alcoholism
- Amputation
- Shingles

Post-herpetic neuralgia is characterized by an idiopathic reactivation of ant damage to nerve fibers.[108] condition in which prolonged y elevated blood glucose and low ainful disorder is complicated by s, the latter leading to focal capillary damage and concomitant hypoxia and nutrient deprivation.[110]

post-herpetic neuralgia—Pain in the area where a shingles infection (caused by the Varicella zoster virus) once occurred. The pain may last for months or years.

Trigeminal neuralgia arises from damage to one or both trigeminal nerves. of intense hyperalgesic and frequently , scalp, forehead, teeth, or jaw geminal neuralgia is typically after common in women.[111] Cold wind, g, and talking can exacerbate the clinical manifestations of trigeminal neuralgia.[112] Patients additionally report sensations of temporary numbness, tingling, and pricking (paresthesias); sensitivity to touch; and muscle weakness.[112]

Trigeminal neuralgia—????

Excruciating episodic pain in the area of the trigeminal nerve, often precipitated by stimulation of well-defined trigger points.

Notes: