Continuing Medical Education

Understanding Pain Mechanisms

Pain can be managed more effectively by studying its pathways.

Goals and Objectives

After reading this article, the podiatrist should be able to:

1) Identify the anatomy of the pain pathway.

2) Understand the different parts of the pain pathway where analgesia can be influenced.

3) Understand how medications can be effective at various points in the pain pathway.

4) Appreciate the importance of choosing appropriate pain medication.

5) Develop a strategy for pain management in both acute and chronic pain.

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*Following this article, an answer sheet and full set of instructions are provided (p. 222).—**Editor***

By Steve E. Abraham DPM and Simon Young, DPM

What is pain? In 1979, the International Association for the Study of Pain defined pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[3] Pain affects every category of patient care. Whether the issue is wound care, a painful joint, an irritated skin condition, or an endocrine disorder, understanding the pathway of pain will help the practitioner in assessment and management of the patient in pain. The pain pathway can be broken into categories to clarify the pain process. Nociception, Transduction, Transmission, Perception, and Modulation are concepts that are basic to understanding the pain pathway.

Nociception

Nociception refers to the process by which information about tissue damage is transmitted from peripheral receptors to the peripheral nervous system and onto the central nervous system. The first step in the pain pathway is the transduction of noxious stimulation into nerve signals that will travel up ascending pathways to the brain. Nociceptors are free, primary afferent nerve endings in cutaneous, muscle, and visceral tissues. Nociceptors can respond in one of two ways. They can respond to the actual noxious stimulation or they can respond to the changes in surrounding tissues caused by the noxious stimulation. Noxious stimulation can cause cellular damage that precipitates cellular changes, including the release of numerous chemicals, enzymes, mediators, ionic changes, pH

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changes, and catalyzing the inflammatory cascade. Histamine and serotonin release increase vasodilation and inflammation.

Transduction

Transduction is the conversion of energy from a noxious thermal, mechanical or chemical stimulus into nerve impulses (electrical energy) by nociceptors. Stimuli evoke changes in the integrity of neural membranes of the nociceptors, producing inward sodium and calcium currents, causing the basic action potential that initiates a nerve impulse.

Transmission

Transmission is the process where neural signals from the site of transduction are transmitted to the spinal cord and brain.

After the nerve impulse is created, the nociceptive impulse is transmitted from the free nerve endings along stimulus-specific nerve fibers. This is the first order nociceptive primary afferent nerve fiber consisting of A-delta fibers and C-fibers. Each carries different types of input and are responsible for different subjective perceptions.

A-delta fibers are small, thinly myelinated neurons. "First Pain" is the initial sensation of pain described as sharp, localized and well defined. A-delta fibers are modality specific. They respond to extremes of temperature, high intensity mechanical stimulation, light and deep pressure, stab and pinch.

C-fibers are small, unmyelinated afferent nerves. The absence of myelin leads to slower conducting velocity. "Second Pain" is a diffuse, poorly localized, burning, throbbing or gnawing sensation after the initial sensations of "first pain." Second pain is temporally and qualitatively distinct from first pain.

Quantitatively, the majority of nociceptive afferent nerve fibers in the cutaneous tissues are C-fibers. C-fibers are polymodal; they can be activated by any combination of thermal, mechanical or chemical stimulation. C-fiber thresholds for stimulation are easily sensitized, accounting for persistent pain and hyperalgesia. C-fibers also innervate muscle tissue, tendons and areas surrounding vascular walls.

In addition to nociceptive initiation of the pain pathway into the primary afferent nerve, neurogenic stimulation can also initiate impulses into the pain pathway.

Neuron to Neuron

The next step in the pain pathway is the passing of the nerve impulse from the primary afferent neuron to the second order neuron in the spinal cord for transmission to the brain. The spinal cord has a ventral and a dorsal root. About 40% of afferent nociceptive nerves synapse in the ventral spinal cord. The vast majority of cutaneous and visceral nociceptive afferent fibers project to the dorsal horn of the spinal cord. The dorsal horn is anatomically divided into ten zones called laminae of Rexed and these laminae are numbered consecutively. Both A-delta fibers and C-fibers end on specific second order neurons in the laminae I, II, IIa, and V of the dorsal horn of the spinal cord. This is the origin of the ascending pathway of the second order neurons to the brain.

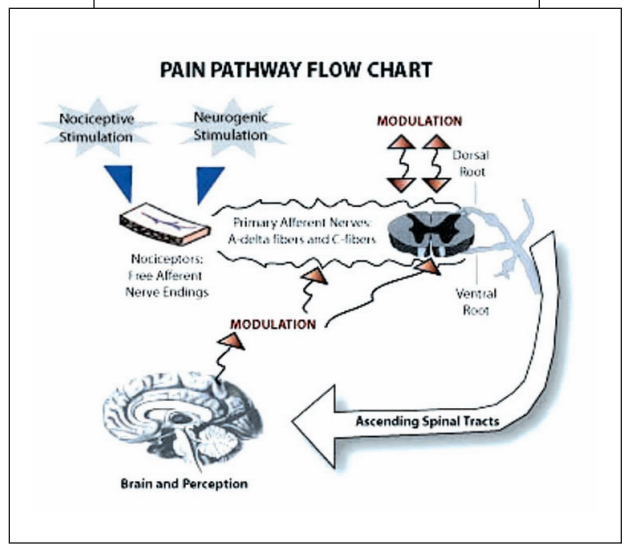

Figure 1

Neurochemical Mediation

The principle neurochemical mediator at the synaptic cleft between the primary afferent neuron and the dorsal horn cells is glutamate. The primary afferent neurons also release a chemical called substance-P which binds to receptors post-synaptically.

The dorsal horn of the spinal cord is a critical site for convergence and neural processing of nociceptive information. The second order neurons aggregate in the dorsal horn, project contralaterally and ascend to the brain in bundles called ascending tracts.

Some second order neurons ascend in the spinothalmic tract to the brainstem, midbrain and thalamus. Others ascend to higher brain centers via the spinoreticular tracts.

The Gate Control Theory

The "gate control" theory of pain involves the convergence of first order neurons at the dorsal horn. Unpleasant impulses entering the dorsal horn via C-fibers can be suppressed by concurrent stimulation of A-delta fibers or by impulses passing through A-beta fibers. This is the basis for acupuncture and for transcutaneous electrical nerve stimulation (TENS).

In summary, first pain is punctuate, well localized and temporally defined. It is a function of nociceptive stimulation of rapidly conducting A-delta primary afferent fibers that synapse in the dorsal horn of the spinal cord with second order neurons. Second pain is more diffuse, longer lasting. It is nociceptive sensation that follows the initial stimulus and is the result of slower conducting C-fibers transmitting signals to the dorsal horn of the spinal cord.

Neurotransmitters mediate transmission of pain in the spinal cord and the brain. There are many neurotransmitters and more are being discovered. They can be categorized as: excitatory neurotransmitters, such as glutamate and tachykinins, inhibitory transmitters, such as gamma amino butyric acid (GABA), and neurotransmitters associated with descending pain transmission, such as noradrenalin, serotonin and opiates.[1]

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.

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Modulation

Modulation is the descending inhibitory and facilitory input from the brain influencing nociceptive transmission at the level of the spinal cord. Modulation actually occurs at many levels, but historically it has been considered only as the attenuation of ascending dorsal horn transmission by descending inhibitory input from the brain. Multiple brain regions contribute to this descending inhibition. Impulses from these brain centers descend and cause the release of inhibitory substances at the dorsal horn of the spinal cord. Some of these inhibitory substances include endogenous opioids, serotonin, norepinephrine and GABA. These inhibitory substances bind on receptors on either the primary afferent neurons or the dorsal horn secondary neurons to inhibit transmission of the nociceptive impulse from the primary afferents to the secondary neurons in the dorsal horn. This endogenous modulation accounts for the wide variations in pain perception in patients with similar injuries.[1]

Neurons of the sensory cortex of the brain can exert inhibitory control over the other neural pathways inside the brain itself. Cortical inhibition can normalize or stabilize afferent neural signals. The cortical neurons can also excite the lower brain pain pathways. Therefore, cortical neurons can discriminately amplify or reduce the afferent pain input to the brain.

In addition to the descending effects of the brain and brainstem, pain modulation also occurs at the spinal cord level. Activation of local circuits within the spinal dorsal horn modulates pain. This is one of basics of the "gate theory" of pain.[1]

Sensitization

There are two types of sensitization in the pain pathways, peripheral sensitization and central sensitization. With peripheral sensitization, sensitized nociceptors exhibit a lower threshold for activation and an increased rate of firing. Inflammatory mediators, intense, repeated, or prolonged noxious stimulation, or both can sensitize nociceptors. Sensitized nociceptors generate nerve impulses more readily and more often.

Central Sensitization

Central sensitization refers to a state of spinal neuron hyperexcitability. For example, repeated or prolonged input from C-nociceptors or damaged nerves causes a longer-lasting increase in dorsal horn neuron excitability and responsiveness that may outlast the initial stimulus by minutes to hours.

Central and peripheral sensitization has several clinical manifestations. Hyperalgesia is an increased response to a noxious stimulus. Allodynia refers to a painful response to a normally innocuous stimulus. Persistent pain is prolonged pain after a transient stimulus. Referred pain is the spread of pain to uninjured tissue. Hyperalgesia and allodynia encourage protection of the injured part during the healing phases. These processes, however, can persist long after the healing of the injury, creating chronic pain. Central Sensitization explains why neuropathic pain often exceeds the provoking stimulus, both spatially and temporally. Central sensitization also explains the longstanding observation that established pain is more difficult to suppress than acute pain.

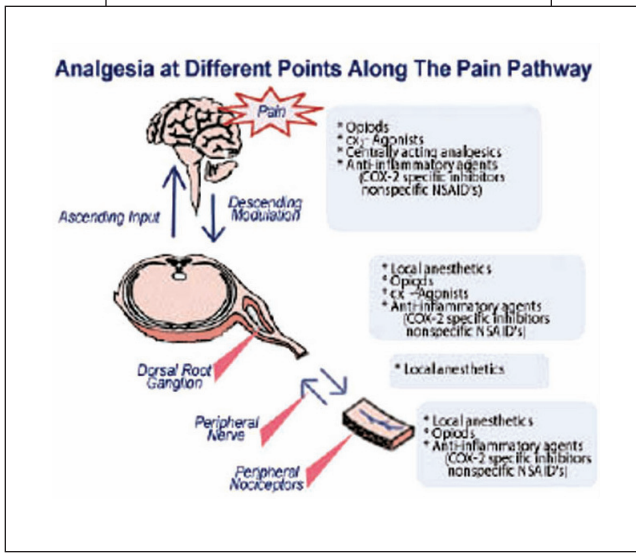

Figure 2

Nociceptive Pain

Pain can be classified based on the presumed underlying pathophysiology. The two major categories of pain are nociceptive and neuropathic. Nociceptive pain is caused by the ongoing activation of A-deltä and C-nociceptors in response to a noxious stimulus (e.g., injury, disease, inflammation). Pain arising from visceral organs is called visceral pain, whereas pain 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.

With nociceptive pain, the assumption is that the nervous system is functioning properly. There is also a close correspondence between the pain perception and the intensity of the stimulus.

Neuropathic Pain

Neuropathic pain (which may result in a decrease in sensation and parasthesia rather than pain) is caused by aberrant signal processing in the peripheral or central nervous system. In contrast to nociceptive pain, 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. Neuropathic pain can be categorized as peripheral or central in origin. Painful peripheral mononeuropathy and polyneuropathy, de-afferentation pain, sympathetically maintained pain, and central pain are subdivisions of these categories. A chronic pain state may occur when pathophysiologic changes become independent of the inciting event.

Pain Classifications

Pain is sometimes classified as either: 1)acute pain 2) chronic pain 3) cancer pain 4) chronic non-cancer pain.

Acute Pain

In terms of duration, pain is considered acute if it lasts less than 3-6 months. Acute pain is associated with relatively high levels of pathology and acute pain usually resolves with the healing of the underlying injury. Acute pain is usually nociceptive, but it may be neurogenic. Biologically, acute pain functions as a warning for injury.

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Chronic Pain

Chronic pain extends 3-6 months beyond the onset of the pain or the expected healing of the injury that caused the pain. With chronic pain, the levels of identified pathology are low and the level of pain is insufficient to explain the presence or the extent of the pain. Chronic pain generally serves no adaptive purpose. It degrades health and function. Chronic pain may be nociceptive, neurogenic or both. Chronic pain may exist without an apparent cause.

Cancer Pain

Pain associated with potentially life-threatening conditions is called "malignant pain" or "cancer pain". There is a strong relationship between tissue pathology and pain levels. Cancer pain has acute and chronic components and multiple etiologies.

Chronic Non-Cancer Pain

Chronic non-cancer pain is a subtype of chronic pain. It is persistent pain not associated with cancer. There is a weak relationship between tissue pathology and pain levels. Chronic non-cancer pain responds poorly to standard treatments. There are many medical/legal and work related issues with chronic non-cancer pain.

Managing Pain by Medication

According to Supernaw[2], the first step in managing pain by medication is to assess the nature and severity of the pain. Is it acute or chronic? Is it benign, malignant, organic, psychogenic? Neuropathic pain is addressed in a different manner than nociceptive pain. Pain should then be graded as mild, moderate, severe, or excruciating.

The therapeutic approach is to match the assessed pain category to the appropriate pharmacotherapeutic agent. According to Supernaw[2], there is no justification for beginning pain therapy with a less potent over-the-counter analgesic before attempting a more potent drug. If the assessment is severe to moderate pain, the patient will not respond to a mild analgesic and there is no justification in trying. This treatment principle illustrates the importance for accurate assessment and categorization of the patient's pain.

Degrees of Pain

Acute pain is classified as mild, moderate, severe or excruciating[2]. Chronic pain has the same elements, but it has more psychological components. Chronic pain has a debilitating effect on the life of the patient, and leads to suffering. An important consideration in treating chronic pain is quality of life issues. In acute pain, simply diminishing the intensity of pain may be enough. The qualities of acute pain itself may help in identifying its underlying cause. With chronic pain, there is no useful purpose, and the quality of life must be considered as well as decreasing the intensity.

Breakthrough Pain

"Breakthrough Pain" is an important concept to understand in the management of pain. This is an episode of pain that breaks through pain that is being relieved by an ongoing analgesic. These episodes are controlled by a short-acting, rapid onset PRN medication.[3]

Pain Medications

Pain medications can be grouped into three categories: non-opioid analgesics, opioid analgesics, and adjuvant analgesics. Non-opioid analgesics include acetaminophen, NSAID's, aspirin and salicylic derivatives. Opioid analgesics include mu opioid agonists and agonist-antagonists. Adjuvant analgesics, like anti-epileptics, tricylcic antidepressants, and local anesthetics are primarily indicated for conditions other than pain.

The mechanism of action of non-opioid analgesics vary. NSAID's inhibit the enzyme cyclooxygenase (COX), resulting in blocking of prostaglandin synthesis. Acetaminophen acts mostly via a central mechanism. All non-opioid analgesics have anti-inflammatory, antipyretic and analgesic effects, except acetaminophen which has negligible anti-inflammatory effect. The analgesic effect of NSAID's is prompt (minutes to hours), whereas the anti-inflammatory effect takes longer (1-2 weeks). Non-opioid analgesics relieve acute and chronic pain, and mild to moderate levels of pain. They are often added to a medication regimen for an opioid-sparing effect (reducing the dose of opioid). Combination therapy with opioids is recommended because the different mechanisms of action offer more pain relief with fewer side effects. Non-opioids do not produce tolerance, physical dependence, or addiction.

Dosage Ceiling

The concept of dosage ceiling means that a dose is reached where additional side-effects occur without any increased pain relief. All non-opioids have a dosage ceiling. NSAID side-effects include: GI problems, bleeding, kidney dysfunction, hypersensitivity reactions and CNS effects. Acetaminophen does not damage gastric mucosa or inhibit platelet aggregation; it provides pain relief comparable to aspirin but has negligible anti-inflammatory activity. Acute or chronic overdose may cause liver or kidney toxicity.

Opioid Mechanism of Action

The mechanism of action of opioid analgesics is by binding to opioid receptors in the CNS and in the periphery. This has three effects: 1) inhibit the transmission of nociceptive input from the periphery to the spinal cord, 2) activate descending inhibitory pathways to modulate transmission in the spinal cord, 3) alter limbic system activity. Opioids modify sensory and affective aspects of pain.

The different actions of opioids (agonist or antagonist) at various opioid receptors (mu, kappa and delta) provide a means of classification. Opioids are broadly categorized as mu agonists or agonist-antagonists. Opioid drugs have a high affinity for mu receptors located at the suprasoinal sites. Mu activation produces analgesia, respiratory depression, euphoria, and physical dependence.[2] Kappa receptors are located within the spinal cord and mediate spinal analgesia, miosis, and sedation.[2] Opioid agonist drugs occupy and activate the opioid receptor. This mimics the effects of natural, endogenous endorphins and enkephalins. The greater the quantity of agonist administered, the greater the level of analgesia and of the adverse effects. Opioid agonists are not limited by a ceiling effect.

Adjuvant Analgesics

Anti-epileptic drugs (AED's) are a type of adjuvant analgesic. Because they reduce membrane excitability and suppress abnormal discharge in neurons that are pathologically damaged, AED's are used for neuropathic pain. AED's work especially well for episodic shooting, stabbing, or knife-like pain

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from peripheral nerve syndromes. Use of AED's for peripheral nerve pain is mostly "off label." Side-effects of AED's include sedation, dizziness, nausea and mental clouding. AED's require close monitoring as some of the more serious side effects include hematological abnormalities, liver dysfunction and hypersensitivity reactions.[3]

Antidepressants have some analgesic properties, and offer some relief of chronic neuropathic pain. Some antidepressants block reuptake of serotonin and norepinephrine in the CNS, increasing the effectiveness of the endogenous pain-modulating pathways.[5] Tricyclic antidepressants (TCA's) are used to treat many types of chronic pain, including headaches, migraines, low back pain, cancer pain, fibromyalgia, and neuropathic pain.[3] The use of TCA's for pain is considered "off label." Side-effects of TCA's include sedation, orthostatic hypotension, dry mouth, blurred vision, constipation and urinary retention. TCA's are relatively contraindicated in patients with conduction abnormalities. Elderly patients are at greatest risk for side effects.[3]

Local anesthetics are another form of adjuvant analgesics. Local anesthetics block sodium channels and inhibit generation of abnormal impulses by damaged nerves.

Mild Pain

Acute mild pain, by definition, is limited in its duration and does not have to be addressed aggressively. Sometimes it does not have to be treated at all, because when the underlying condition passes, the pain ends. Chronic mild pain, by definition, is long-term and non-pharmacological, pain-mitigating therapy sometimes works. First-line analgesics include aspirin and acetaminophen.

Aspirin

Aspirin was first introduced to the U.S. in 1899 and has analgesic, anti-inflammatory, anti-platelet and antipyretic activity. Its mechanism of action is by inhibiting prostaglandin synthesis. Aspirin is given as a 650 mg. dose every 4 hours[2] for mild, pain-related problems. Aspirin is absorbed rapidly in the duodenum; it is metabolized in the liver and is highly albumin-bound. Oral anticoagulants (OAC) are 97% albumin-bound, and aspirin displaces the OAC from its inactive binding site, thereby causing an increase in the active dose of the OAC. Aspirin is effective in mild to mild-moderate pain. It has many risks, including severe gastrointestinal irritation and ulceration, hearing loss and blood-related problems. Aspirin is contraindicated for infants and children into their teens because it is implicated in Reye's syndrome.[2]

Acetaminophen

Acetaminophen is a choice for patients who cannot tolerate aspirin. It has analgesic and antipyretic activity. For patients who have gastrointestinal- related complications, acetaminophen is better tolerated than aspirin. Acetaminophen has only weak anti-inflammatory activity. The only significant adverse reaction is hepatotoxicity, if acetaminophen is taken over extended periods of time.[2] Acetaminophen should not be taken by patients with diminished liver function or with alcoholic problems, or by those with significant kidney damage. For adults, dosing guidelines are 325-650 mg every 4-6 hours, not to exceed 4g./day for acute pain.[2]

Dosage ceiling means that a dose is reached where additional side-effects occur without any increased pain relief.

OTC NSAID's

There are three OTC non-steroidal anti-inflammatory agents that can be used as second line pharmacotherapy for acute or chronic mild pain. They are ibuprofen, naproxen sodium and ketoprofen.

Ibuprofen

Ibuprofen was first introduced in the U.S. in 1969[2]. In 1984 the 200 mg. dose became OTC. It has analgesic, anti-inflammatory, some anti-pyretic, and some anti-platelet activity. It works by decreasing tissue concentration of prostoglandins. The OTC dose of 200 mg. has little anti-inflammatory effect; its primary effects are analgesic and anti-platelet adhesion. Its most common side effect is GI pain and ulceration and this is dose-related. Ibuprofen should not be taken by patients who are subject to asthma caused by aspirin, have peptic ulcer disease, have a bleeding disorder, a blood cell disorder, or have significant kidney damage. Even though ibuprofen appears to be especially helpful in menstrual cramps, one of its adverse reactions is altering the pattern and timing of the menstrual cycle. [2]. It is not recommended in the last 3 months of pregnancy.

Naproxen Sodium

Naproxen sodium was introduced in the U.S. in 1974 and approved for OTC use in 1994. It has analgesic, anti-inflammatory, some antipyretic, and some anti-platelet activity. It works by decreasing tissue concentrations of prostaglandins. Naproxen sodium has a lower incidence of adverse effects than other NSAID's; however, patients need to be warned of the same adverse effects as those with ibuprofen and other NSAID's.

Naproxen sodium is also especially helpful with menstrual cramps but it can also alter the pattern and timing of the menstrual cycle. In its OTC dose it has minimal anti-inflammatory activity.

Ketoprofen

Ketoprofen was approved in 1995 for OTC. Ketoprofen is in the same category as ibuprofen and naproxen sodium and in its OTC dose also has minimal anti-inflammatory activity.

Moderate Pain

When the intensity of pain reaches the moderate level, the dose of aspirin, acetaminophen, ibuprofen, naproxen sulfate, or ketoprofen is increased as the third-line therapy.[2] A low dose of OTC medication will diminish the patient's appreciation, so the clinician should begin therapy at a dose corresponding to the patient's pain level. The dose of aspirin is increased from 650 mg to 1,000 mg. When increasing doses of NSAID's, prescription levels are given.

With increasing dosing levels of NSAID's, the likelihood of adverse effects are increased. GI irritation is the most common. Patients should

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be instructed to take NSAID's with a full glass of water and not to lie down for 30 minutes after dosing. A small amount of food may be taken with the NSAID's.

Cox-2 Inhibitors

COX-2 inhibitors are a category of NSAID's that selectively inhibit the COX 2 enzyme. They inhibit the cascade that converts substrates to prostaglandins that enhance pain transmission and provoke inflammation, but they do not block prostaglandins that cause platelets to aggregate and do not block the production of prostoglandins that protect the gastrointestinal mucosa. The safety of COX-2 inhibitors, however, resulted in Vioxx and Bextra being removed from the market and Celebrex dosage adjusted.

An important point to remember is that an individual who is sensitive to one NSAID will generally be sensitive to all NSAID's. It is the responsibility of the clinician to recommend discontinuing an NSAID before GI-related problems lead to significant GI bleeding.

The next direction to take with moderate pain is to use opioids and opioid combinations. A first choice would be a combination of aspirin or acetaminophen with codeine. When codeine is added, the side-effects of opiates must be considered.

Opioid Drugs

The opioid drugs work by binding to and activating specific receptors in both the central and peripheral nervous system. The three important opioid receptors are mu, kappa and delta. Mu activation produces analgesia, respiratory depression, euphoria and physical dependence. Mu receptors are located in supraspinal sites. Kappa receptor activation produces spinal anesthesia, miosis and sedation. Kappa receptors are located in the spinal cord. Delta receptor activation produces analgesia. Their importance is still being investigated.

Opioid agonist drugs occupy and activate the opioid receptors, thereby mimicking the natural effects of endogenous endorphins and enkephalins. There is no ceiling effect with agonists. The greater the quantity of agonists administered, the greater the analgesia and side effects. GI side-effects are the most bothersome; they include constipation, gastric distress and nausea.

Bulk-forming laxatives do not help with constipation from opioid agonists. Stimulant or irritant laxatives are necessary to promote GI motility. Sedation can occur and patients need to be warned when driving or operating machinery. patients need to be warned that there is also an additive depressant effect when alcohol is consumed with an opioid agonist.

One interesting observation about codeine is that even though it is an effective agonist, doses above 65 mg. do not produce added benefit, but the complications, especially constipation, significantly increase.

Codeine Combinations

If, with moderate chronic pain, codeine and codeine-like combinations are not satisfactory Tramadol could be considered. Tramadol activates mu receptors and inhibits norepinephrine reuptake. Tramadol has less affinity for opioid receptors as compared to other opioids and therefore cannot be given in combination with other opioids. Tramadol can be used for neuropathic pain, but its effects are delayed and it must be used for a 10-day trial before its effectiveness can be judged.

Severe Pain

More potent pharmacotherapy is needed for severe pain. Morphine sulfate is the standard for parenteral narcotics. Morphine is a pure agonist, which attaches to the narcotic receptors and activates them fully. Agonists do not have a therapeutic ceiling (except codeine). The greater the amount administered, the more narcotic receptors occupied and the greater the analgesia. It is never acceptable to use more than one type of narcotic because of the nature of receptor occupation.

A mixed agonist-antagonist would occupy both receptors. Even though it activates only the kappa receptor, it blocks the mu receptor. Adding an agonist to a regimen that contains an agonist or a mixed agonist-antagonist would not only not enhance the anesthesia, but might diminish the therapeutic analgesia.[3]

Acute Severe Pain

Treatment for acute severe pain differs from other types of pain treatment. Usually the pain practitioner begins at a relatively low dose and gradually increases to higher doses or adds other drugs until the condition is managed. In acute severe pain the drug regimen should be equal to the level of pain. The dose administered is one that is felt to be adequate to relieve the acute, severe pain. Subsequent doses can be tapered down until the pain threshold is discovered. The patient is rapidly brought to a level of comfort.[4]

Summary

Pain is a debilitating medical and psychological problem. The management of pain requires an understanding of both basic and advanced principles that cross the boundaries of differing medical specialties. Knowledge and understanding are the tools for managing pain and suffering. ■

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EXAMINATION

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See answer sheet on page 223.

1) The first step in the pain pathway, the conversion of stimulus into nerve impulses by nociceptors, is called:
   A) transduction
   B) transmission
   C) perception
   D) modulation

2) The first order nociceptive primary afferent nerve fiber includes:
   A) a-delta fibers
   B) beta lactam rings
   C) C-fibers
   D) a and c

3) The vast majority of cutaneous and visceral nociceptive afferent fibers project to which part of the spinal cord?
   A) ventral root
   B) dorsal root
   C) peripheral nociceptor
   D) primary afferent

4) Unpleasant impulses entering the dorsal horn via C-fibers can be suppressed by concurrent stimulation of A-delta fibers or by impulses passing through A-beta fibers. This theory has been called:
   A) Transmediation theory
   B) Arche of Bloch theory
   C) Gate theory
   D) Young's tripolar theory

5) The descending inhibitory and facilitory input from the brain influencing nociceptive transmission at the level of the spinal cord is called:
   A) Frequency alteration
   B) Modulation
   C) Maturation
   D) Protein substitution

6) This term refers to a painful response to a normally innocuous stimulus:
   A) Allodynia
   B) Hyperalgesia
   C) Referred pain
   D) Persistent pain

7) This term refers to an increased response to a noxious stimulus:
   A) Allodynia
   B) Hyperalgesia
   C) Referred pain
   D) Persistent pain

8) When sensitized nociceptors exhibit a lower threshold for activation and an increased rate of firing, the concept is called:
   A) Transcription
   B) Peripheral sensitization
   C) Central sensitization
   D) None of the above

9) The type of pain that reflects nervous system injury or impairment is called:
   A) nociceptive pain
   B) neuropathic pain
   C) a and b
   D) neither a or b

10) The levels of identified pathology are low and the level of pain is insufficient to explain the presence or the extent of the pain. This refers to which type of pain:
   A) acute pain
   B) chronic pain
   C) cancer pain
   D) chronic non-cancer pain

11) When pain is being controlled by an analgesic and an episode occurs where there is a sudden increase or breakthrough in the level of pain, this concept is called:
   A) cell-mediated pain
   B) Wallerian degeneration
   C) Breakthrough pain
   D) Bloch pain

12) This concept means that a dose is reached where additional side effects occur without any increased pain relief:
   A) ceiling dose
   B) "hit the wall" dose
   C) breakout dose
   D) titrated dose

13) This medication was first introduced to the U.S. in 1899 and has analgesic, anti-inflammatory, anti-platelet and antipyretic activity.
   A) acetaminophen
   B) ibuprofen
   C) aspirin
   D) naproxen

14) The three important opioid receptors are:
   A) Mu
   B) kappa
   C) delta
   D) all of the above

15) A drug introduced in the U.S. in 1969 that has a 200mg OTC dose and has analgesic, anti-inflammatory, some antipyretic and some anti-

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EXAMINATION

(cont'd)

platelet activity is called:

A) Ketamine
B) Ibuprofen
C) Succinylcholine
D) Pyruvic acid

16) With increasing dosing levels of NSAID's the likelihood of adverse effects are:

A) decreased
B) increased
C) remains the same
D) does not change

17) The GI effects of opioids that are most bothersome include:

A) constipation
B) gastric distress
C) nausea
D) all of the above

18) Doses above 65 mg. of this drug do not produce added benefit, but the complications, especially constipation, significantly increase:

A) barbiturates
B) codeine
C) lidocaine
D) ketamine

19) The drug that is the standard for parenteral narcotics that is a pure agonist and that attaches and fully activates narcotic receptors is:

A) Tramadol
B) Tolnaftate
C) Morphine Sulfate
D) Dexamethasone sulfate

20) Free, primary nerve endings in cutaneous, muscle and visceral tissues are called:

A) nociceptors
B) raptors
C) Young's corpuscles
D) Bloch mediators

See answer sheet on page 223.

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Card #_____Exp. Date_____

Note: Credit card is the only method of payment. Checks are no longer accepted.

Signature_____Soc. Sec.#_____Daytime Phone_____

State License(s)_____Is this a new address? Yes_____ No_____

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Over, please

ENROLLMENT FORM & ANSWER SHEET (cont'd)

EXAM #4/07
Understanding Pain Mechanisms (Abraham and Young)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

LESSON EVALUATION

Please indicate the date you completed this exam

_____

How much time did it take you to complete the lesson?

_____ hours _____minutes

How well did this lesson achieve its educational objectives?

_____Very well _____Well

_____Somewhat _____Not at all

What overall grade would you assign this lesson?

A B C D

Degree_____

Additional comments and suggestions for future exams:

_____

_____

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_____

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