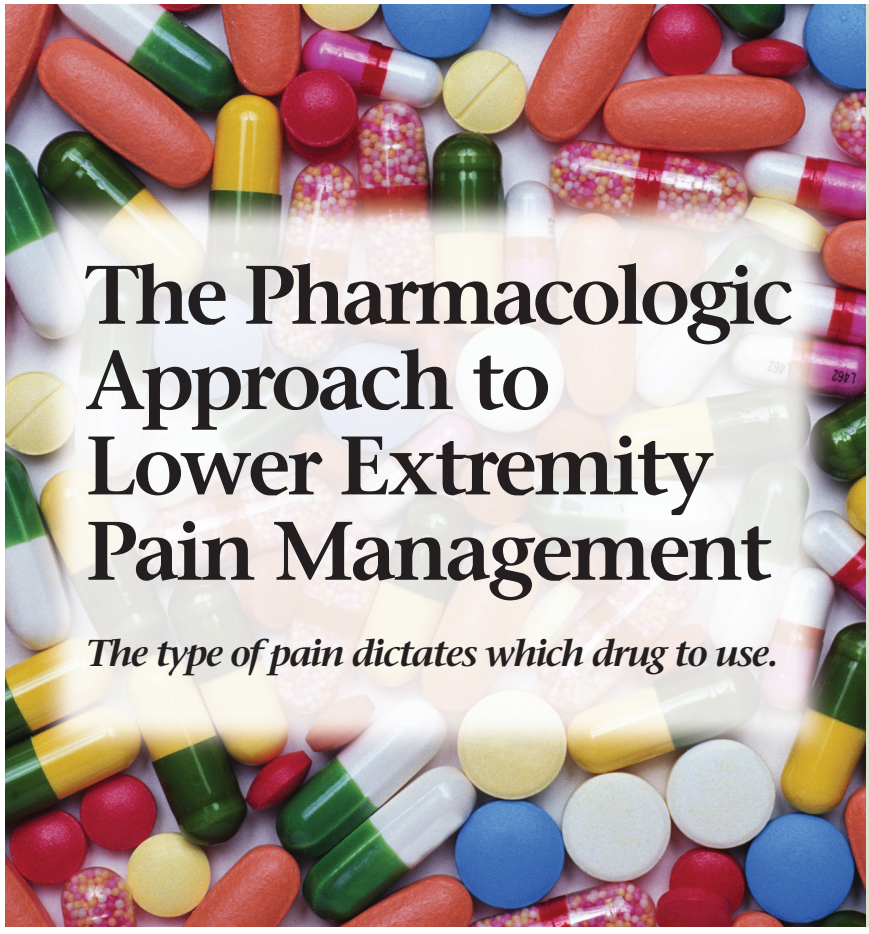
Continuing Medical Education



The Pharmacologic Approach to Lower Extremity Pain Management

The type of pain dictates which drug to use.

Goals

1) To recognize the necessity for the development of a pain management protocol to address an unmet need regarding the treatment of painful conditions of the lower extremity.

2) To further appreciate the pharmacologic treatment options in the armamentarium of the podiatric physician.

Objectives

After completing this CME, the reader should:

1) Appreciate the mechanism of action for different types of pain so that a clinically-based treatment plan can be instituted.

2) Appreciate the pharmacologic options available for the outpatient treatment of inflammatory pain.

3) Appreciate the pharmacologic options available for the outpatient treatment of neuropathic pain.

4) Appreciate the pharmacologic options available for the outpatient treatment of functional pain such as fibromyalgia.

5) Have received a review of the efficacy of different medications used to treat pain in the lower extremity.

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*Following this article, an answer sheet and full set of instructions are provided (p. 190).—**Editor***

By Bryan D Caldwell, DPM, MS

PhotoDisc

Podiatric medicine is about to experience an explosion. It will not be a destructive event, but rather an explosion of patients filling your waiting rooms. Is it due to an epidemic of plantar fasciitis, a pandemic of onychomycosis, or an endemic of hallux abductovalgus? No, the increase in patient volume will be due to a condition that most consider a symptom, not a disease; but it's time that we label this problem for exactly what it is.

Pain is a disease. True, it ac-

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companies many other maladies that we treat, but the time has come to separate it from all other problems and realize that pain, regardless of its etiology, can be treated even if we are not 100% sure of its origin. Although pain is treated in this way by other specialties, podiatric medicine has yet to fully appreciate its place in the alleviation of pain as a disease and its importance in the area of pain management.

Serious pain affects over 75 million Americans. Each year another 25 million experience acute pain as a result of injury or surgery according to the American Academy of Pain Medicine. The treatment of chronic pain exceeds 100 billion dollars a year, according to the National Institutes of Health. By actively treating pain as a disease, our practices will serve a great need for the relief of acute and chronic pain of the lower extremities, and easily increase volume in the double digit percentages over the next 10 years and beyond.

A physician's role is to prevent, remove, or reduce suffering. To adequately treat pain, podiatric physicians must view pain as we do other diseases of the lower extremities. Although we may not have a definitive treatment for the pain disorder in all cases, we still can alleviate suffering by having a basic understanding of the distinct forms of pain. Pain can be divided into the two major categories of nociceptive pain and neuropathic pain.

By actively treating pain as a disease, our practices will serve a great need for the relief of acute and chronic pain of the lower extremities, and easily increase volume in the double digit percentages over the next 10 years and beyond.

I prefer dividing it into four separate disorders as a way to successfully treat it in the clinical setting. These distinct subtypes are nociceptive pain, inflammatory pain, neuropathic pain, and functional pain.

Nociceptive Pain

Nociceptive pain can be viewed as the body's early warning system. It is an internal alarm that protects us from harmful temperatures, caustic chemicals, and a variety of other hazards that may cause injury. If one grabs a hot object, it is the nociceptive pain pathways that alert the person to let go. Nociceptive pain is a necessary protective mechanism and is not the focus of a pain management protocol.

Chronic inflammation serves as precursor for chronic pain.

Inflammatory Pain

Inflammatory pain is characterized by the development of hypersensitivity. Although inflammation is critical for the delivery of leukocytes to an injured area, leukocytes can unfortunately prolong inflammation and induce further injury by the release of toxic metabolites and proteases into the extracellular space.[1]

This results in pain and inflammation for an extended period of time. Although this may serve to protect an area from further harm, it can often linger and cause unnecessary suffering. A patient who sustains an ankle sprain may have tenderness in the lateral collateral ligament area for an extended period following injury, and the podiatric physician can play an integral part in alleviating this pain.

Under typical circumstances, there is then resolution of the inflammatory pain as chemical mediators are removed and leukocyte emigration ends. If substantial destruction is the result of the inflammation or if the inflammation has occurred in a tissue that does not regenerate, scarring and/or fibrosis may ensue. Scarring and fibrosis may convert an acute problem into a chronic one. Chronic inflammation serves as precursor for chronic pain. Instead of neutrophilic infiltration characteristic of acute inflammation, macrophages, plasma cells, and lymphocytes permeate the area.[1] These mononuclear cells lead to further destruction.

While inflammation initially is a necessary and important part of healing, it must be controlled so that it does not produce further damage. This can be done with simple actions such as PRICE therapy which consists of protective measures, rest, ice, compression, and elevation. These simple measures can often halt the inflammatory process and the pain associated with it before it becomes a chronic problem. It is important to start this therapy early; but, by the time the patient reaches our offices, the condition is well past the point of resolution with simple measures.

When damage occurs in an area, phospholipids in the cell membrane of injured cells produce arachidonic acid by the action of the enzyme phospholipase. Arachidonic acid is further degraded by lipooxygenase and cyclooxygenases 1 and 2 (COX-1, COX-2) to produce a variety of leukotrienes and prostaglandins.

Prostaglandin E2 (PGE2) is responsible for pain and inflammation. The key to the resolution of inflammatory pain, at this point, is by blocking the production of PGE2.

Hence, the primary pharmacologic solution to the treatment of acute inflammatory pain and to the disruption of the chronic in-

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flammatory pain cycle is the nonsteroidal anti-inflammatory drug (NSAID). NSAIDs are excellent analgesics. Although each NSAID may have slightly different properties, no clinically significant difference in efficacy exists among specific drugs.[2]

NSAIDs block the cyclooxygenase enzyme and therefore the production of PGE2. Non-selective NSAIDs block both COX-1 and COX-2. Examples are fenoprofen, ibuprofen, diclofenac, and naproxen. COX-2 specific inhibitors, such as celecoxib, preferentially block the COX-2 enzyme only. The incidence of gastrointestinal problems are higher with the non-selective agents compared with the COX-2 specific ones; but cardiovascular issues have been a recent concern with certain COX-2 inhibitors presumably due to an imbalance between prostacyclin, a vasodilator and inhibitor of platelet aggregation, and thromboxane, a vasoconstrictor and promoter of platelet aggregation. Furthermore, COX-2 inhibitors offer no gastrointestinal advantage over non-selective NSAIDs if the patient is also taking aspirin.[3]

The key to the resolution of inflammatory pain, at this point, is by blocking the production of PGE2.

Neuropathic Pain

Neuropathic pain management is certainly an area where the podiatric physician can play an integral part and podiatric physicians will see an even greater opportunity to alleviate this type of pain in the future. It is understood that neuropathic pain is a condition in which we see an over-excitation of the nervous system. On a global level, neuropathic pain seems to be a consequence of an imbalance between glutamate, an excitatory neurotransmitter, and gamma alpha butyric acid (GABA), an inhibitory neurotransmitter; but at an anatomic level one can observe a more fascinating picture.

Codeine/ acetaminophen is a poor choice for effective pain management.

Remember that peripheral nerve fibers are made up of three types. A-beta fibers are large, myelinated sensory fibers and are not responsible for pain, but instead are responsible for normal sensation only. A-delta fibers are thin myelinated pain fibers that transmit faster, sharp pain. C fibers are thin unmyelinated fibers that transmit a slow dull ache. A-beta fibers travel separately from the pain-transmitting C fibers.

Anatomically, researchers have shown that when injury occurs, A-beta fibers sprout into the C fibers, creating a large myelinated super highway for pain to be transmitted from the periphery to the central nervous system. This sets the stage for neuropathic pain; and thus something that normally would not hurt begins to cause pain.[4]

Five Components

When treating neuropathic pain it is helpful to divide the pain process into its five components. The five components are transduction, conduction, transmission, perception, and modulation. Podiatric physicians can manage painful neuropathic conditions primarily by targeting the conduction of the nerve impulse by specific sodium channels, the transmission of the nerve impulse across the spinothalamic tract neuron in the dorsal horn of the spinal cord with the release of glutamate and substance P, the modulation of serotonin, norepinephrine, and endorphin release from the brainstem, or the modulation of calcium influx in hyperexcited neurons.

Conduction

Conduction of the nerve impulse by sodium channels can be blocked with a variety of medications, one of which is a very effective topical treatment. The 5% lidocaine patch is FDA approved for treating postherpetic neuralgia, but can be used for a variety of pain syndromes from low back pain to diabetic peripheral neuropathy. Three randomized controlled studies have shown statistically significant relief of pain.[5]

Up to three patches are used just proximal or directly over the painful site for 12 hours and then removed for 12 hours. Off-label these patches can be used for up to 24 hours quite safely. The author has used these quite effectively for symptomatic relief of pain from arterial ulcers, for neuropathic pain relief, and for chemotherapy-induced pain management.

Transmission

Transmission of the nerve impulse, and therefore pain, can be blocked by opioids. Opioids are morphine-like medications that bind to mu receptors and block the release of substance P (preparation). It is important to choose the right narcotic medication, because there are certain ones that have no place in a pain management program. Propoxyphene should have no place in pain management and studies confirm that it should have no place in pain relief whatsoever. The 1994 Agency for Healthcare Research showed that propoxyphene was no better than a placebo. This was later confirmed by a 1997 meta-analysis showing that Darvon (propoxyphene/aspirin) and acetaminophen was no better than acetaminophen alone.[6]

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Essentially these studies prove that those physicians who are using Darvocet (propoxyphene/acetaminophen) for pain relief are actually managing their patients' pain with acetaminophen alone. Furthermore, propoxyphene is associated with dizziness and its metabolite is cardiotoxic.

Codeine/acetaminophen is also a poor choice for effective pain management. By comparison, this pain medication is less effective and has the most side-effects of any of the other pain relief medications. Constipation is also a frequent problem. In addition, since codeine is a prodrug and 10% of the population does not have the enzyme to convert codeine to morphine, a large percentage of your practice will see absolutely no pain relief with the use of codeine/acetaminophen. If one compares fenoprofen, an effective non-selective NSAID, with codeine for pain relief, there is some evidence that fenoprofen is a better pain reliever that the 60 mg. dosage of codeine/acetaminophen (Tylenol #4).[7]

Topical capsaicin is another medication that can be used to control pain levels by blocking transmission.

Meperidine

Meperidine (Demerol) should not be used in a pain management program because it is only effective for two hours and is the highest peaking narcotic. This is not preferable because the patient remains in pain throughout most of the dosing regimen and when pain is fully relieved, the patient is in a state of euphoria. Meperidine is more toxic than other agents and its efficacy is poor when compared to other agents such as morphine.

Better choices for the management of pain are oxycodone/acetaminophen (Percocet, Tylox), hydrocodone/acetaminophen (Vicodin, Lortab), and tramadol (Ultram, Ultracet). Tramadol is frequently used for acute or chronic pain, but it has also been shown to be an effective agent for the treatment of neuropathic pain.[8]

Tramadol should be avoided in patients who are currently taking tricyclic antidepressants, slow serotonin reuptake inhibitors, and other opioids due to a potential increased risk of seizures. Time-released morphine (MS Contin) and time released oxycodone (Oxycontin) are both effective in the treatment of neuropathic pain. Although these narcotics have the potential for physical dependence and, in rare instances, addiction, judicious use of opioids can be very effective for the relief of pain that has not responded to other agents.

Topical Capsaicin

Topical capsaicin is another medication that can be used to control pain levels by blocking transmission. While it was once thought that pain relief with capsaicin was due to a decrease in substance P, research in neurochemistry suggests that capsaicin provides pain relief by the modulation of excitatory amino acid activity and possibly by degradation of the substance Preceptor.[9,10] The biggest problem with commercially available forms of capsaicin is that the percentages are very low. Still, consistent use can provide pain relief for those patients who cannot tolerate oral medications.

NSAIDs

If NSAIDs are the primary medications for the treatment of inflammatory pain, the anticonvulsants are the primary agents for the relief of neuropathic pain. It was once thought that these medications worked by blocking the sodium channel, but it is now believed that the mechanism of action for the anticonvulsant is by modulating calcium influx in hyperexcited neurons. Gabapentin and pregabilin bind to the alpha 2 delta subunit of neuronal calcium channels, thereby reducing the release of substance P, glutamate, and norepinephrine.[11,12]

Gabapentin has a maximum FDA approved dosage of 2400 mg, but much higher dosages have been used off-label and appear to be safe. The issue that must be determined with gabapentin lies in its own pharmacokinetics. As the dosage of gabapentin is increased, its concentration in the plasma increases disproportionately. The bio-availability of an oral dose of gabapentin is only 60% at a dosage of 900 mg and decreases steadily as the dosage is increased so that only 1/3 of the medication is available at a dosage of 3600 mg.[13]

In the past, it had been quite common to see patients taking 300 mg. each night. We now know that the 300 mg dosage of gabapentin is no better than placebo in the relief of neuropathic pain.[14]

Pregabalin, however, has a much better pharmacokinetic profile and has proven to be quite superior in the relief of neuropathic pain when compared to gabapentin. A linear pharmacokinetic profile and bio-availability of greater than 90% at all oral dosages places this anticonvulsant at the top of the algorithm for the treatment of painful neuropathic syndromes. Dosing for painful peripheral neuropathy of 75 mg. bid to 150 mg. bid is effective.[13]

Pregabalin has proven to be quite superior in the relief of neuropathic pain when compared to gabapentin.

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Enhancement of Modulation

When we consider the management of pain by the enhancement of modulation, the prototypical medication for the relief of neuropathic pain is the tricyclic antidepressant (TCA). TCAs keep norepinephrine and serotonin from being degraded, thereby prolonging the inhibition of nerve impulse transmission. TCAs may actually also work as sodium channel blockers and by blocking the N-methyl D-aspartate (NMDA) receptor, the binding site for glutamine.

Patients with diabetes mellitus are said to have impairment in the generation of the vasodilator nitric oxide.

It must be understood that not all TCAs are exactly alike and some are better suited for a pain management program. Although it was one of the first TCAs to be used for neuropathic pain relief, amitriptyline is the worst choice due to its side-effect profile.

All TCAs have anticholinergic side-effects such as drowsiness and dry mouth, but amitriptyline has the most reported. For this reason, TCAs such as desipramine and nortriptyline are better choices.[15]

The starting dosages are 10-25 mg. at bedtime and can be titrated to a target of 25-150 mg. Having said that, one must remember that TCAs are not FDA-approved for the treatment of neuropathic pain, offer no better than 50% improvement in only about 50% of patients, and probably should be used as a second line drug for patients who have failed on anticonvulsants. There is some evidence to suggest a potential analgesic effect from the topical TCA, doxepin, for neuropathic pain.[16]

One randomized study suggests that bupropion, an aminoketone derivative unrelated to the TCAs, may be a suitable alternative as it has a more favorable side effect profile.[17] This medication is FDA-approved for major depressive disorders and is also used as an adjunct therapy for smoking cessation.

Another medication that has been shown to be effective and was actually the first drug to be approved for painful peripheral neuropathy is duloxetine. Duloxetine is a serotonin norepinephrine reuptake inhibitor (SNRI) that proved to be safe and effective in two randomized controlled studies. It works by potentiating modulation at a dosage of 60 mg twice a day.[18]

Duloxetine is a SNRI, not a slow serotonin re-uptake inhibitor (SSRI). Evidence suggests that SSRIs such as sertraline and fluoxetine are not effective.[19]

Other medications specifically designed to counteract signal transduction pathways such as ruboxistaurin, the protein kinase C inhibitor, will offer further treatment options for the podiatric physician who treats patients who have diabetes mellitus.[20] Ruboxistaurin has shown symptomatic improvement in randomized controlled trials.[21]

Potentiation of Nitric Oxide

Another place that may deserve attention for the treatment of painful diabetic neuropathy is in the potentiation of nitric oxide levels. Patients with diabetes mellitus are said to have impairment in the generation of the vasodilator nitric oxide. Monochromatic infrared therapies have shown promise in the relief of pain secondary to diabetic neuropathy, presumably by increasing levels of nitric oxide. At least one small trial with the use of isosorbide dinitrate (ISDN) spray has shown reduced pain scores when compared to the use of placebo.[22,23]

Functional Pain

The final subset of clinical pain is known as functional pain and is called such because it has no clear peripheral pathology. An example of functional pain is the pain associated with fibromyalgia. TCAs may offer some amelioration of pain severity[24] The combination of an NSAID and a tricyclic antidepressant (TCA) has shown benefit. Duloxetine, the norepinephrine serotonin re-uptake inhibitor, has also shown evidence of improvement of symptoms.[25] Some podiatric physicians are also claiming remarkable results with rebalancing of the body's biomechanics in patients who suffer from fibromyalgia.

Pain Management Algorithms

The podiatric physician can develop his or her own pain management algorithm to treat pain effectively. First-line therapy for inflammatory pain should center on the NSAIDs such as fenoprofen, naproxen, and diclofenac; while first line therapy for neuropathic pain is most appropriately the anticonvulsant pregabilin along with the 5% lidocaine patch and/or capsaicin.

Opioids should be considered as second or third-line therapy for both inflammatory and neuropathic pain management.

Second-line therapy for both inflammatory and neuropathic pain involves treatment with tramadol. The NSRI duloxetine should also be considered as a second-line therapy for the treatment of neuropathic pain. Physical dependence does occur with the use of prolonged opioid treatment, but the benefits of pain relief outweigh this risk if other therapies have been unsuccessful.

Opioids should be considered as second or third-line therapy for

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Pain...

both inflammatory and neuropathic pain management. Due to anticholinergic side effects, TCAs should be categorized as second or third-line therapy for neuropathic pain. Ancillary pain relief modalities such as TENS units and monochromatic infrared therapy can be used in conjunction with any other pharmacologic treatments.

Conclusion

Pain management will soon become a larger and larger percentage of our practices. On the one hand, as the baby boomers live longer and demand a lifestyle that is far more active that their predecessors, the number of acute and chronic inflammatory pain cases are certain to rise. Many of these will involve the lower extremity or present in the lower extremity from more proximal sites such as the lumbar spine. On the other, as more of our nation's children and young adults continue to become obese due to lack of exercise and poor nutritional habits, we will see an epidemic of diabetes mellitus Type 2 and its subsequent consequences such as painful peripheral neuropathy.

Now more than ever, we as a profession should take our place in the field of pain management. Regardless of whether we make a conscious choice to do so, it will soon be a part of the practice of every podiatric physician. ■

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Pain management will soon become a larger and larger percentage of our practices.

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EXAMINATION

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See answer sheet on page 191.

1) Which of the following pain medications has been shown to be no more effective at relieving pain than placebo?
- A) Codeine
- B) Diclofenac
- C) Fenoprofen
- D) Propoxyphene

2) Which of the following pain medications is ineffective in 10% of the population due to an enzyme deficiency?
- A) Codeine
- B) Diclofenac
- C) Fenoprofen
- D) Oxycodone

3) What protein kinase C inhibitor shows promise for the treatment of diabetic neuropathy?
- A) Duloxetine
- B) Nortriptyline
- C) Ruboxistaurin
- D) Tramadol

4) What is the proposed global mechanism for the development of painful neuropathic syndromes?
- A) An imbalance between prostacyclin and thromboxane
- B) An imbalance between glutamate and GABA
- C) An imbalance between substance P and neurokinin 1
- D) An imbalance between serotonin and norepinephrine

5) Which of the following medications is considered first line therapy and the best choice for the treatment of neuropathic pain?
- A) Gabapentin
- B) Duloxetine
- C) Imipramine
- D) Pregabilin

6) Which of the following medications is considered first line therapy for the treatment of acute inflammatory pain?
- A) Diclofenac
- B) Fenoprofen
- C) Naproxen
- D) All of the above

7) Which narcotic is not a preferred medication for a pain management program due to its short duration and its tendency to produce euphoria?
- A) Hydrocodone
- B) Hydromorphone
- C) Meperidine
- D) Morphine

8) Identify the biggest problem with the use of tricyclic antidepressants in the treatment of chronic pain?
- A) Anticholinergic side effects
- B) Diarrhea
- C) Nausea
- D) Urinary incontinence

9) Which norepinephrine serotonin reuptake inhibitor is FDA approved for the treatment of painful diabetic neuropathy?
- A) Duloxetine
- B) Fluoxetine
- C) Nortriptyline
- D) Ruboxistaurin

10) What non-narcotic topical therapy in the form of a patch is useful for the treatment of neuropathic pain?
- A) Ethinyl estradiol/norelgestromin
- B) Fentanyl
- C) Lidocaine
- D) Nicotine

11) What dosing is recommended for the treatment of painful peripheral neuropathy with pregabilin?
- A) 25-50 mg. bid
- B) 75-150 mg. bid
- C) 175-225 mg. bid
- D) 250-300 mg. bid

12) What bid dosing regimen is recommended for the treatment of painful diabetic neuropathy with duloxetine?
- A) 15 mg.
- B) 30 mg.
- C) 45 mg.
- D) 60 mg.

13) COX-2 inhibitors have been shown to cause less gastrointestinal ulcerations when compared to non-selective NSAIDs. What negates this advantage?
- A) The concurrent use of aspirin
- B) The concurrent use of cimetidine
- C) The concurrent use of misoprostol
- D) The concurrent use of omeprazole

14) Some evidence exists to support the theory that an NSAID may offer better pain relief than certain narcotics. Which of the following is true according to previously published literature?
- A) Fenoprofen 200 mg. was considered better at relieving post-operative pain than 60 mg. codeine.
- B) Fenoprofen 200 mg. was considered better at relieving post-operative pain than 8 mg. morphine.
- C) Diclofenac 50 mg. was considered better at relieving post-operative pain than 60 mg. codeine.
- D) Diclofenac 50 mg. was considered better at relieving post-operative pain than 8 mg. morphine.

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EXAMINATION

(cont'd)

15) What peripheral nerve fibers are responsible for the transmission of pain?
- A) A beta and A delta fibers
- B) A beta and C fibers
- C) A delta and C fibers
- D) A beta, A delta, and C fibers

16) Why is it likely that podiatric physicians will see an increase in the number of cases of painful diabetic neuropathy over the next decade?
- A) The increase is due to young patients with corticosteroid-induced diabetes mellitus.
- B) The increase is due to more cases of young patients that are obese.
- C) The increase is due to more cases of young patients with virally-induced pancreatic endocrine dysfunction.
- D) The increase is due to more cases of young patients with Leprechaunism.

17) Name a disease that represents functional pain.
- A) Fibromyalgia
- B) Morton's neuroma
- C) Plantar fasciitis
- D) Post-herpetic neuralgia

18) What is presumably increased with the use of monochromatic infrared therapy?
- A) Atrial natriuetic factor
- B) Nitric oxide
- C) PDGF
- D) Serotonin

19) What is the most common side-effect with the use of codeine?
- A) Constipation
- B) Diarrhea
- C) Drowsiness
- D) Lactorrhea

20) What is the typical starting dosage for treating painful diabetic neuropathy with a tricyclic antidepressant?
- A) 1-2 mg.
- B) 10-25 mg.
- C) 50-75 mg.
- D) 100-150 mg.

See answer sheet on page 191.

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Enrollment/Testing Information and Answer Sheet

Continuing Medical Education

Note: If you are mailing your answer sheet, you must complete all info. on the front and back of this page and mail with your credit card information to: ***Podiatry Management*, P.O. Box 490, East Islip, NY 11730.**

TESTING, GRADING AND PAYMENT INSTRUCTIONS

(1) Each participant achieving a passing grade of 70% or higher on any examination will receive an official computer form stating the number of CE credits earned. This form should be safeguarded and may be used as documentation of credits earned.

(2) Participants receiving a failing grade on any exam will be notified and permitted to take one re-examination at no extra cost.

(3) All answers should be recorded on the answer form below. For each question, decide which choice is the best answer, and circle the letter representing your choice.

(4) Complete all other information on the front and back of this page.

(5) Choose one out of the 3 options for testgrading: mail-in, fax, or phone. To select the type of service that best suits your needs, please read the following section, "Test Grading Options".

TEST GRADING OPTIONS

Mail-In Grading

To receive your CME certificate, complete all information and mail with your credit card information to:

Podiatry Management
P.O. Box 490, East Islip, NY 11730

There is **no charge** for the mail-in service if you have already enrolled in the annual exam CPME program, and we receive this exam during your current enrollment period. If you are not enrolled, please send $20.00 per exam, or $139 to cover all 10 exams (thus saving $61* over the cost of 10 individual exam fees).

Facsimile Grading

To receive your CPME certificate, complete all information and fax 24 hours a day to 1-631-563-1907. Your CPME certificate will be dated and mailed within 48 hours. This service is available for $2.50 per exam if you are currently enrolled in the annual 10-exam CPME program (and this exam falls within your enrollment period), and can be charged to your Visa, MasterCard, or American Express.

If you are *not* enrolled in the annual 10-exam CPME program, the fee is $20 per exam.

Phone-In Grading

You may also complete your exam by using the toll-free service. Call 1-800-232-4422 from 10 a.m. to 5 p.m. EST, Monday through Friday. Your CPME certificate will be dated the same day you call and mailed within 48 hours. There is a $2.50 charge for this service if you are currently enrolled in the annual 10-exam CPME program (and this exam falls within your enrollment period), and this fee can be charged to your Visa, Mastercard, American Express, or Discover. If you are not currently enrolled, the fee is $20 per exam. When you call, please have ready:

1. Program number (Month and Year)
2. The answers to the test
3. Your social security number
4. Credit card information

In the event you require additional CPME information, please contact PMS, Inc., at **1-631-563-1604**.

ENROLLMENT FORM & ANSWER SHEET

Please print clearly...Certificate will be issued from information below.

Name _____ Soc. Sec. #_____
Please Print: FIRST MI LAST

Address_____

City_____State_____Zip_____

Charge to: _____Visa _____ MasterCard _____ American Express

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_____

Check one: _____ I am currently enrolled. (If faxing or phoning in your answer form please note that $2.50 will be charged to your credit card.)

_____ I am not enrolled. Enclosed is my credit card information. Please charge my credit card $20.00 for each exam submitted. (plus $2.50 for each exam if submitting by fax or phone).

_____ I am not enrolled and I wish to enroll for 10 courses at $139.00 (thus saving me $61 over the cost of 10 individual exam fees). I understand there will be an additional fee of $2.50 for any exam I wish to submit via fax or phone.

Over, please

ENROLLMENT FORM & ANSWER SHEET (cont'd)

EXAM #6/07
The Pharmacologic Approach to Lower Extremity Pain Management (Caldwell)

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:

_____

_____

_____

_____

_____

_____