

**INSIDE THIS ISSUE****CASE STUDY****Managing Diabetic Peripheral Neuropathic Pain****Steven A. King, MD****6****What's Hot in Pain Control****8****ASK THE EXPERT****10****Learning Objectives**

After reading the three-part newsletter series for 2005, participants should be able to:

- Differentiate chronic pain from acute pain and describe the mechanisms of pain and sites of activation
- Address common barriers that limit effective pain management for patients with chronic pain
- Determine the recommended components for comprehensive assessment of pain and function in patients with chronic pain
- Select more varied pharmacologic and nonpharmacologic strategies for initial and ongoing management of chronic pain
- Describe therapeutic approaches to minimize potential adverse effects and drug interactions and identify safety issues and precautions

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## Treating Chronic Pain: Biopsychosocial Approach in Primary Care Practice

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The complexities inherent in any chronic disease, including chronic pain syndromes, suggest that clinical management is best addressed from a biopsychosocial point of view. In essence, the biopsychosocial model attempts to understand and promote patient care from a perspective that encompasses biological, psychological, and social phenomena.<sup>1</sup> In this article we aim to discuss some tips and suggestions that can be

applied in the primary care setting to increase awareness and lead to better documentation of each of the contributors to the experience of chronic pain.

**Goal Setting**

What is the goal of chronic pain management? Is it to feel better? Function better? Do physicians and patients agree on these points? There is a dearth of literature on

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## Arthritis and the COX-2 Conundrum: A Case Study

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Donald is a 70-year-old former high school teacher who had been enjoying an active retirement. He has osteoarthritis (OA) of the hip and knee, which was confirmed some years previously by radiography. He was until recently using celecoxib at 200 mg OD or at 200 mg BID as required and was very satisfied with the level of pain relief. Recently Donald's wife has stopped him from using this medication in the light of recent news reports and FDA warnings on the safety of celecoxib and other COX-2 inhibitors. Now his arthritis pain has increased considerably and is restricting his mobility. He is very reluctant to resume therapy with a COX-2 inhibitor and wishes to know whether he can gain satisfactory pain relief by other means. Donald has a history of mild heart failure, mild renal impairment, and mild dyspepsia.

**How would you educate Donald about taking COX-2 inhibitors?**

Recently raised concerns over the safety of selective COX-2 inhibitors have created a dilemma for patients and physicians alike. The COX-2 inhibitors (celecoxib, rofecoxib, and valdecoxib) have become a standard treatment for OA pain because of their relative lack of gastrointestinal side effects compared with traditional NSAIDs such as naproxen,

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## EDITOR'S PERSPECTIVE ON PAIN

Many primary care physicians practice a biopsychosocial approach to care. They seek to understand their patients in the context of their lives and emotional status. When facing difficult clinical issues or challenging patients, however, there may be a tendency to focus on the problem at hand and address it from a limited perspective. Such may be the case when working with patients who experience chronic pain, especially if the pain is poorly controlled.

The multitude of issues involved in caring for patients with pain often becomes a discussion of:

- How much pain is present
- How well drug therapy is working
- Parameters for continued prescription of medication

In addition, providers may feel pressure from their perceptions of time, legal, or "cure" considerations. By definition, chronic pain implies a clinical circumstance that will be a long-term problem and will not be easily resolved. Unfortunately, physicians may identify success or failure as it relates to complete resolution of pain.

This newsletter's article by Drs Passik and Kirsh is an important reminder that management of such patients requires a thoughtful strategy, which:

- Enhances a beneficial doctor-patient relationship
- Incorporates an appreciation of patients' circumstances
- Involves a multifaceted approach to pain control
- Supports the patients' physical, social, and emotional functions

The authors also emphasize that this approach provides the best opportunity for benefit. Furthermore, they offer a direct, goal-setting plan ("the 4 As") which can be used in busy practice settings to support both physicians and patients in their desire to improve quality of life.

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This educational activity is a component of the NIPC® and is designed to heighten the knowledge of physicians and other healthcare providers about the serious impact of unresolved pain on patient care. Some of the agents included in this newsletter are discussed in the context of uses for which they have not been approved by the FDA.

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The National Initiative on Pain Control® (NIPC®) is an integrated CME education initiative that was established in 2001 to help physicians improve outcomes for their patients who have pain.

Living with pain has deleterious effects on many aspects of the patient's life, including deterioration of physical functioning, the development of psychological distress and psychiatric disorders, and impairment of interpersonal functioning. Of special concern, less-than-optimal training of physicians in pain disorders has led to the underassessment and undertreatment of patients who are living with pain. The program heightens physician awareness of the impact of pain on patient's daily living in terms of quality of life, lost workdays, and societal/familial consequences.

NIPC addresses the barriers to achieving pain control by providing potential pathways for action and expected amelioration of their patients' pain. By providing physicians with the latest advances and strategies in pain management, they will be better able to translate clinical data into clinical practice.

All NIPC programs are developed and continuously evaluated by the NIPC Education Council, an expert, multidisciplinary team of specialists, researchers, and practicing physicians in pain management. The NIPC Faculty includes nationally respected experts in the pain management field.

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## Arthritis and the COX-2 Conundrum:

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ibuprofen, and diclofenac. The COX-2 inhibitors have the convenience of once-daily dosing and also higher subjective impressions for pain relief than standard NSAID therapy, even if this is not reflected in clinical trial endpoints. Unfortunately, recent placebo-controlled trials of high-dose COX-2 inhibitors for prevention of Alzheimer's and colorectal polyps had to be stopped because of greater-than-placebo rates of myocardial infarction (MI) and stroke. More significantly for OA patients, the findings led to a hurried re-examination of the use of COX-2 inhibitors for treating pain. Rofecoxib and valdecoxib have been voluntarily withdrawn by the manufacturers, and celecoxib, while remaining available in pharmacies, is being subjected to new scrutiny on cardiovascular safety.<sup>1</sup>

The observed increase in serious cardiovascular side effects seems to be associated with high or very high doses and is probably due to the perturbation of the balance between thromboxane, which causes clumping of platelets and vasoconstriction, and prostacyclin, which works in opposition to this process. The selective COX-2 inhibitors may lead to the disproportionately low production of prostacyclin and potential complications may occur. Thus, a bal-

ance between thromboxane and prostacyclin is desirable.

Additional clinical trials focusing on safety of COX-2 inhibitors are under way. In all likelihood, the end result will be additional warnings placed on prescribing information of COX-2 inhibitors in the context of higher doses or warnings about their use in patients at higher risk of MI or stroke. In the meantime, uncertainty remains over the magnitude of risk incurred when COX-2 inhibitors are used to treat OA and RA patients. RA patients are perhaps at somewhat greater risk, as not only are they at greater risk of cardiovascular disease to begin with, but they are often treated with higher doses of COX-2 inhibitors.

### How would you manage Donald?

The approach to treating Donald described here exemplifies the balance that must be struck between therapeutic benefit and risk of side effects while we still have limited information. Donald has moderate cardiovascular risk factors including mild, controlled hypertension. While clearly not in the risk category of a post-MI patient, a prudent approach to avoiding drug-related cardiovascular risk is imperative here.

### NSAID Therapy

One possible approach to treatment is the use of traditional (non-COX-1 sparing) NSAIDs, which has risks of its own. Many patients cannot tolerate long-term therapy with these drugs because of gastrointestinal side effects. The patient described here experiences occasional dyspepsia and may be prone to further side effects with conventional NSAIDs. Another very important concern is the risk of serious hemorrhage as a result of ulceration. Our patient has an elevated risk of NSAID-induced side effect due to age, and his risk may be still greater if he had a prior history. Yet another concern is that traditional NSAIDs may share some of the same cardiovascular side effects as COX-2 inhibitors. This was demonstrated in the ADAPT study that was stopped early because naproxen might have been contributing to a 50% increase in MI and stroke over placebo. While the drug has since been vindicated at FDA panel hearings,<sup>1,2</sup> overall, there is new concern that NSAIDs inhibit bone and tendon

healing and little clinical safety justification exists for switching a patient's medication from a COX-2 inhibitor to a nonselective NSAID.

One other approach is to combine a nonselective NSAID with a gastroprotective agent, either misoprostol or a proton-pump inhibitor. Both the American College of Rheumatology and American Pain Society recommend this approach for OA patients with GI risk factors if a COX-2 inhibitor is ineffective. Donald, as described here, has some risk because of his mild dyspepsia.

### What alternative treatment can be offered to Donald?

Selected intra-articular glucocorticoids may be valuable for the treatment of moderate-to-severe pain due to OA. Indeed, the ACR identifies them as an additional approach to an oral agent as a treatment for moderate-to-severe OA. This procedure should be used cautiously, especially if repeated. Another therapy is intra-articular injection of hyaluronan, a procedure known as viscosupplementation. There are four

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## Alternative Treatments for Osteoarthritis

Intra-articular injection

Cognitive-behavioral strategies

Exercise

Attain/maintain ideal weight

Physical/occupational therapy

Assistive devices

Massage

Glucosamine

Nonselective NSAID with

- Misoprostol or
- Proton-pump inhibitor

Topical therapy

- Capsaicin
- Lidocaine patch 5%

Surgical intervention

## Latest News

For the latest medical information on safety concerns of COX-2 inhibitors and oral nonsteroidal anti-inflammatory drugs (NSAIDs) in management of chronic pain and arthritis, refer to these Web sites.

[www.fda.gov/cder/drug/infopage/COX2/NSAIDdecisionMemo.pdf](http://www.fda.gov/cder/drug/infopage/COX2/NSAIDdecisionMemo.pdf)

[www.fda.gov/cder/drug/InfoSheets/HCP/NSNSAIDsHCP.pdf](http://www.fda.gov/cder/drug/InfoSheets/HCP/NSNSAIDsHCP.pdf)

[www.fda.gov/ohrms/dockets/ac/05/minutes/2005-4090M1\\_Final.htm](http://www.fda.gov/ohrms/dockets/ac/05/minutes/2005-4090M1_Final.htm)

[www.arthritis.org/conditions/NSAIDs/Straight\\_Talk\\_FAQ.asp](http://www.arthritis.org/conditions/NSAIDs/Straight_Talk_FAQ.asp)

[www.fda.gov/fdac/features/2005/205\\_pain.html](http://www.fda.gov/fdac/features/2005/205_pain.html)

[www.rheumatology.org/public/factsheets/nsaids.asp](http://www.rheumatology.org/public/factsheets/nsaids.asp)

## Treating Chronic Pain

*Continued from page 1*

how patients set goals for pain management, and whether they and their pain physicians see eye-to-eye on them. It is well known that cancer pain patients are often satisfied with low levels of pain relief.<sup>2,3</sup> We are just beginning to understand that results from a complex combination of expectations, relationship issues (ie, not wanting to distract the physician from treating their disease), goals of care, and previous experiences with relief of pain.

Little is known about these issues in chronic noncancer pain. Some patients will realize functional gains (eg, return to jobs that they love, resume activities) with low levels of pain relief. Others will maintain that they cannot function (eg, return to jobs that they loathe) until they get nearly 100% pain relief. Overall, there is little doubt that it would be hard for a patient to understand the need for compliance, exercise, pacing, and counseling as parts of pain treatment unless we work to bring them on board and they understand their pain management goals. Just as the goal of diabetes therapy is not simply a lowered blood sugar, the goal of pain management is not simply pain relief measured on a 0 to 10 scale. The goal of chronic pain management is to enable people with pain to live a full and rewarding life in spite of a chronic illness.

### Building Motivation

It is important to understand the social and cultural dynamic between physician and patient.<sup>4</sup> Physicians must also be aware of the increasing influence of the Internet and other information sources on the patient-physician relationship. These resources can be an aid in some instances and be a cause for constant challenging of medical decisions and recommendations in others.<sup>5</sup> In addition, clinicians must realize that their conception of what entails "good health" rarely coincides with the beliefs of the patients.<sup>6</sup> Also, there is a great deal of mistrust on the part of patients concerning why treatments are prescribed and the importance of patient adherence or lack thereof.<sup>7</sup>

Thus, there are many barriers for physicians to providing standard health-care, let alone playing the role of moti-

vator for behavioral change. Healthcare practitioners are rarely trained in communications techniques or the psychological tenets that underpin behavioral modification<sup>8</sup> (see Figure). However, this need can be remedied through the use of relatively simple techniques. In a recent study, Dowell and colleagues found that training physicians to hold extended consultations with nonadherent patients to explore the patients' beliefs about their medications and illness had a positive impact on adherence, even 3 months after the intervention had ceased.<sup>9</sup> However, it must be noted that this interaction is difficult to accomplish because of one important factor: time. With an average of 15.4 minutes for a general office visit,<sup>10</sup> it is difficult to accomplish these lofty aims.

### Monitoring Progress and Compliance

The problem with the goals of pain management as stated above is that they are too overarching and vague to monitor and understand day by day. These goals require translation so the success or failure of pain treatment can be measured and communicated from doctor to patient. The use of a systematic approach, such as monitoring the 4 A's (see below), can be useful for monitoring patients and promoting compliance.

### The 4 A's

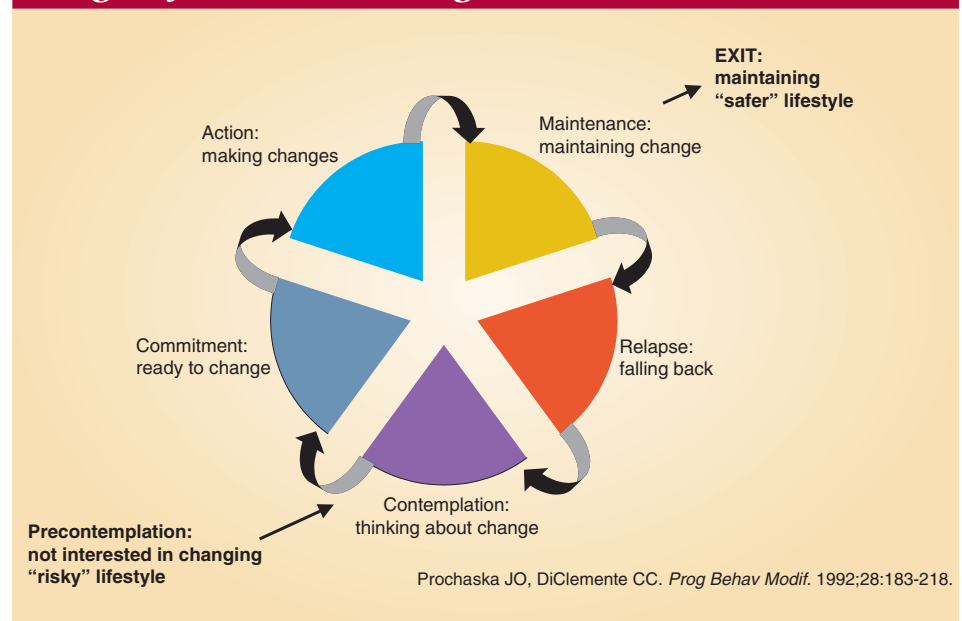
At the University of Kentucky, we devised a useful mnemonic device for

## Successful outcome in pain therapy does not end with the provision of pain control.

following the relevant domains of outcome for pain management.<sup>11</sup> The so-called 4 A's (analgesia, activities of daily living, adverse events, and aberrant drug-taking behaviors) are the clinical domains that reflect progress toward the larger goal of a full and rewarding life. A successful outcome in pain therapy must provide meaningful relief but does not end solely with the provision of pain control. Analgesia must make a true difference in the patient's life, and it must be accompanied by stabilization or improvement of psychosocial and physical functioning, manageable side effects (that do not compromise important areas of functioning), and acceptable drug taking.

Initially developed as a means for clinicians to monitor and document their patients' progress, the 4 A's are not solely intended for the clinician's benefit. They are also useful for explaining the goals of therapy to patients and for helping them understand the larger goal of being treated for pain management. Questions that can be asked in each domain are listed in the Table. Helping the patient to understand the need to reach goals in

## Stages of Behavioral Change



each area can help in planning specific interventions for overcoming obstacles in any of the individual domains. Sometimes, such intervention will require referral to a specialist (ie, referral to a pain clinic if analgesia does not improve or to a psychologist if activities of daily living are hampered by depression or anxiety).

**Conclusion**

Treating chronic pain effectively is challenging and demands a great deal of attention and motivation on the part of the treating physician. Today we realize that chronic pain constitutes a complex mixture of biological factors interacting with numerous psychological, social, and cultural factors. The treating clinician must be ever vigilant and be thorough in assessing the needs and drives of patients.

**References**

1. McDaniel S, Hepworth J, Dogerty W. A new prescription for family health care. *Family Therapy Networker*. 1993;17:18-29.
2. Dawson R, Spross JA, Jablonski ES, Hoyer DR, Sellers DE, Solomon MZ. Probing the paradox of patients' satisfaction with inadequate pain management. *J Pain Symptom Manage*. 2002;23:211-220.
3. Passik SD, Kirsh KL. Probing the paradox of patients' satisfaction with inadequate pain management. *J Pain Symptom Manage*. 2002;4:361-363.
4. Greiner KA. Patient-provider relations—understanding the social and cultural circumstances of difficult patients. *Bioethics Forum*. 2000;16:7-12.
5. Johnson GL, Ramaprasad A. Patient-physician relationships in the information age. *Mark Health Serv*. 2000;20:20-27.
6. Ogden J, Baig S, Earnshaw G, et al. What is health? Where GPs' and patients' worlds collide. *Patient Educ Couns*. 2001;45:265-269.
7. Elwyn G, Edwards A, Britten N. "Doing prescribing": how might clinicians work differently for better, safer care. *Qual Saf Health Care*. 2003;12 (suppl 1):i33-i36.
8. Teutsch C. Patient-doctor communication. *Med Clin North Am*. 2003;87:1115-1145.
9. Dowell J, Jones A, Snadden D. Exploring medication use to seek concordance with 'non-adherent' patients: a qualitative study. *Br J Gen Pract*. 2002;52:24-32.
10. Bensing JM, Roter DL, Hulsman RL. Communication patterns of primary care physicians in the United States and the Netherlands. *J Gen Intern Med*. 2003;18:335-342.
11. Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. *Adv Ther*. 2000;17:70-80.

**PAIN AWARENESS**

**September Is Pain Awareness Month**

A Congressional mandate declared 2000 to 2010 as the Decade of Pain Control and Research. September is Pain Awareness Month in this, the fifth year of that decade. See the Fall issue of PAIN MANAGEMENT TODAY® to learn more about current understanding of pain management, pain research, and treating pain more effectively.



**The 4 A's of Pain for Patient Assessment**

ASSESSMENT DOMAIN	RED FLAGS	DESIRED OUTCOME	SUGGESTED QUESTIONS/TOPICS
<b>Analgesia</b>		<ul style="list-style-type: none"> <li>Determine how much relief it takes for a patient to feel that their life is meaningfully changed                             <ul style="list-style-type: none"> <li>- not necessarily the most important outcome in pain management</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>What is your pain (0-10 scale) most days? At its worst? At its best?</li> <li>What percentage of pain relief have you experienced (0%-100%)?</li> <li>Is the pain relief you have experienced significant to you?</li> </ul>
<b>Activities of daily living</b>	<i>Assess for:</i> <ul style="list-style-type: none"> <li>Physical functioning</li> <li>Family and social relationships</li> <li>Mood</li> <li>Sleep patterns</li> </ul>	<ul style="list-style-type: none"> <li>Patients must understand it is necessary that they comply with all of their recommended treatment options</li> <li>The goal is to help them return to work or leisure activity                             <ul style="list-style-type: none"> <li>- opioids do not fix the myriad problems (deconditioning, obesity, chronic fatigue, drug/alcohol/tobacco use) that must be addressed if the goal is a full and healthy life</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>How would you rate your current quality of life?</li> <li>Have you increased your functionality on treatment?</li> </ul>
<b>Adverse Side Effects</b>	<i>Assess for:</i> <ul style="list-style-type: none"> <li>Constipation, sedation, nausea/vomiting, dry mouth, respiratory depression, confusion, urinary retention, itching, and decreases in testosterone</li> </ul>	<ul style="list-style-type: none"> <li>Patients must be made aware of the adverse side effects inherent in the treatment of their pain condition with opioids and other medications</li> <li>Side effects must be aggressively managed so that sedation and other side effects do not overshadow the potential benefits of drug therapy</li> </ul>	<ul style="list-style-type: none"> <li>Are you able to tolerate your current pain relievers?</li> <li>Are you experiencing any side effects from your current pain relievers?</li> <li>What is the severity of the side effect(s) you are experiencing (mild, moderate, severe)?</li> </ul>
<b>Aberrant Drug-Taking Behaviors</b>	<i>Assess for:</i> <ul style="list-style-type: none"> <li>Negative mood change</li> <li>Purposeful oversedation</li> <li>Requests for early renewals</li> <li>Increases in dose without authorization</li> <li>Reports of loss or theft of prescriptions</li> <li>Doctor shopping</li> <li>Using medications to treat stress or to sleep</li> <li>Asking for medications by name</li> </ul>	<ul style="list-style-type: none"> <li>Even an overall good outcome in every other domain might not constitute satisfactory treatment if the patient is not compliant</li> <li>Dispensing pain medicine in a highly structured fashion (ie, a week's worth at a time) may become necessary</li> <li>Refer to a pain specialist when a pattern of aberrancy emerges or you feel uncomfortable</li> </ul>	<ul style="list-style-type: none"> <li>Patients must be educated about the parameters of acceptable drug taking</li> <li>Assess aberrant behaviors in an open and straightforward manner</li> </ul>

# Managing Diabetic Peripheral Neuropathic Pain:

## CASE-BASED TREATMENT OPTIONS



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**Neuropathy is a common problem associated with diabetes mellitus (DM), occurring in at least 50% of patients with this disorder.<sup>1</sup> Diabetic neuropathies can present in a variety of forms, including loss of sensory and motor function. Pain is one of the more common symptoms. The following is a case report on Joseph, a patient with diabetic peripheral neuropathic pain (DPNP), highlighting treatment options and the management of comorbid depression.**

Joseph is a 52-year-old man with type 2 DM who had been diagnosed with this disease 2 years before being referred by his primary care physician to a pain service. He was referred after he began complaining of bilateral distal lower extremity pain that was diagnosed as being secondary to the DM. Over the course of the treatment of the patient by the pain service, he also reported depression related both to the pain and the impact the DM was having on his life.

### How would you start treatment for Joseph's pain?

There are now two drugs approved by the FDA for the treatment of DPNP – duloxetine and pregabalin\*, both of which were approved in the latter part of 2004. However, other medications have also been demonstrated to provide analgesia for DPNP.

Because the patient's pain was well localized, it was decided to initiate treatment with lidocaine patch 5%.<sup>†</sup> Although this medication is only FDA approved for the treatment of postherpetic neuralgia pain, there is research indicating that it is effective for DPNP.<sup>2</sup> A significant advantage of this medication is the limited potential for side effects because it is a topical medication. Although (as with all analgesics) the exact mechanism by which it provides pain relief remains unclear, it is believed that it works primarily through its action on sodium channels.

### What other treatment can be offered to Joseph?

The patient did receive sufficient relief for several months with the lidocaine patch 5% but the pain then began to increase. At that point, the decision was made to add either an antidepressant or an anticonvulsant. (Although few studies have examined

the use of polypharmacy in the management of neuropathic or other forms of chronic pain, multiple medications are often utilized in clinical practice.) Neither duloxetine, which is an antidepressant, or pregabalin, an anticonvulsant, were FDA approved at the time. [See page 8 for more information.] The medications that were considered were a tricyclic antidepressant (TCA), venlafaxine, and gabapentin, all of which have been demonstrated to be effective for DPNP.<sup>3†</sup>

Because the patient was also beginning to complain of depression, it was decided to start him on an antidepressant to treat both this problem and the pain with a single medication. Antidepressants that inhibit both serotonin and norepinephrine reuptake, including the TCAs, venlafaxine, and duloxetine, appear to provide markedly more analgesia than selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine, and sertraline.<sup>4</sup>

The antidepressants appear to provide analgesia through the modulating effects of serotonin and norepinephrine, both peripherally and centrally. Since the patient is over age 50, the use of TCA was contraindicated because of potential side effects. He was therefore started on extended-release venlafaxine in addition to continuing with the lidocaine patch 5%. Treatment was initiated at 37.5 mg qd and titrated up to a minimal therapeutic dose of 150 mg qd over the next 2 weeks, with no drug-drug interaction.

### Is there a new approach to augment response via different mechanisms of action?

There is limited literature indicating whether an anticonvulsant such as pregabalin or gabapentin or an antidepressant such as duloxetine or venlafaxine should be the first choice as a systemic medication

in the management of DPNP or other neuropathic pain in the absence of depression. The only studies comparing these classes found that gabapentin and amitriptyline, a TCA, were equally efficacious for neuropathic pain.<sup>5</sup> Like the antidepressants, the anticonvulsants appear to provide analgesia through both peripheral and central actions. In neuropathic pain disorders, gabapentin is hypothesized to be an alpha<sub>2</sub> delta calcium channel antagonist.

Unfortunately, few combinations of medications have been systematically studied, and of these, most involve small trials without adequate controls. In this double-blind, randomized, crossover trial comparing monotherapy and combination therapy with active placebo (lorazepam), Gilron et al reported that a combination of gabapentin and morphine provided better pain relief than either medication alone in reducing pain and pain-related disability in 35 patients with DPNP.<sup>6</sup>

### Were Joseph's psychological issues associated with less successful treatment outcome?

Over time, the patient reported an increase in pain and the venlafaxine was gradually increased to an eventual dose of 450 mg qd. This medication continued to provide a sufficient antidepressive effect but his pain continued to be a problem. He was started on gabapentin at an initial dose of 100 mg tid. The patient reported some analgesia from a dose of 300 mg tid. However, the patient reported oversedation at doses above this.

As Joseph was continuing to complain of pain, it was decided to add an opioid, as these can also provide analgesia for neuropathic pain.<sup>7</sup> The patient was started on immediate-release oxycodone 10 mg q4h prn. He reported pain relief with oxycodone taking it round-the-clock, so he was converted to controlled-release oxycodone, as long-acting opioids are indicated when patients are taking an immediate-release preparation on a regular basis for an extended period. The patient was started on controlled-release oxycodone at 20 mg q12h. Over the next 6 months, the dose was increased as the pain worsened. Eventually, the dose reached 120 mg q8h. However, even at this dose, the patient required breakthrough dosing of hydromorphone. At that point, it was decided to switch to an alternative opioid.

In addition to continuous-release oxycodone, the three other commonly used long-acting opioids are transdermal fentanyl patch, controlled-release morphine preparations, and methadone. More recently, a controlled-release form of hydromorphone has become available.

All may be effective, and there are no comparison studies indicating which would be best for neuropathic pain. Methadone was chosen because, alone among the opioids, it has dual action. It is both a mu opioid receptor agonist, like oxycodone, morphine, and fentanyl, and an NMDA receptor antagonist. There is literature indicating that the latter effect may offer additional analgesia.<sup>8</sup> Because the patient had some degree of tolerance due to his extended use of oxycodone, he was started on methadone 20 mg q8h. (Patients who are opioid naive or on lower doses of another opioid should be started at 5-10 mg q8h.) Although methadone has a long half-life of 16 to 24 hours, its analgesic effect lasts 6 to 8 hours, requiring that it be given on a tid to qid schedule for effective pain relief.

The patient received effective analgesia with the combination of methadone, gabapentin, venlafaxine, and lidocaine patch 5%. He was able to tolerate this combination without any problem. Pharmacologic treatment for chronic pain may consist of a number of agents. "Rational polypharmacy" is a term commonly used for the systematic approach to selecting one or more classes of agents for treating neuropathic pain such as peripheral diabetic neuropathy or postherpetic neuralgia. The rationale of additive pharmacotherapy is based on complementary mechanisms of action and synergistic drug effects.

### How should the depression be addressed?

The majority of patients with chronic pain suffer from some form of depression.<sup>9</sup> It is a frequent problem among patients with DPNP, who have to cope not only with the pain, but also the issues related to the diabetes itself and the impact it can have on functioning and lifestyle.

Because of time constraints and the discomfort that some healthcare providers have in discussing psychological issues with patients, the depression may be overlooked. However, in light of research indicating that chronic pain can be exacerbated by depression, the depression should be addressed.<sup>10</sup> It is therefore important to at least inquire about depression. Though self-administered psychological instruments such as the Beck Depression Inventory can be used, the results must be carefully evaluated, as most contain questions about somatic complaints and therefore may provide false diagnoses of depression in patients with physical health problems. Because DM is often a progressive disease and circumstances can change, the depression should be monitored on an ongoing basis.

Psychotherapy and antidepressant medications are the mainstay for the treatment of depression. A combination of the two appears to provide optimal benefit. Physicians who do not have the time or training to provide psychotherapy should consider a referral to a mental health specialist who has experience treating patients

with chronic pain. Joseph was provided supportive psychotherapy in addition to medication management.

As discussed above, antidepressants that also provide analgesia (duloxetine, venlafaxine, TCAs) should be used to treat the depression. At the full doses used to treat depression, the TCAs (eg, amitriptyline) have the highest profile of side effects. Joseph was initially treated with extended-release venlafaxine. He received a good antidepressant effect from this medication, but after he had been on it for more than a year, the depression worsened. Over time, patients can become less responsive to specific antidepressants. As the patient was already on a relatively high dose of 450 mg qd at the time, and because duloxetine had become FDA approved, he was switched to duloxetine. The patient reported an improvement in his depression.

### Conclusion

This case illustrates some of the issues encountered in treating patients with the pain of peripheral diabetic neuropathy. It is apparent that further research remains to be performed to determine which combination of medications provide optimal analgesia. Many medications may be beneficial for pain control in patients with diabetes and this approach is not limited to DPNP, but can be applied to a variety of other chronic pain conditions.

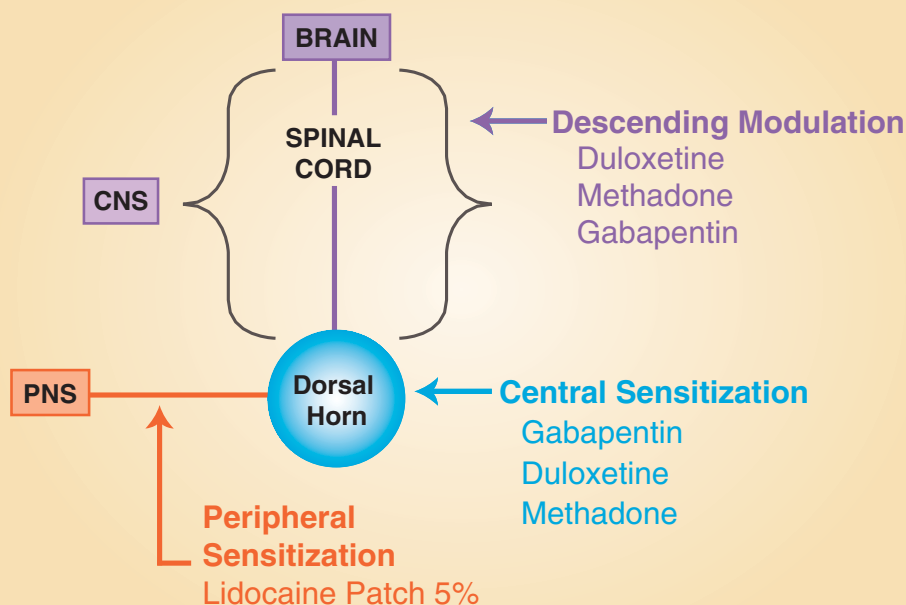
### References

1. Vinik AI, Mehrabyan A. Diabetic neuropathies. *Med Clin North Am.* 2004;88:947-999.
2. Barbano RL, Herrmann DN, Hart-Gouleanu S, Pennella-Vaughan J, Lodewick PA, Dworkin RH. *Arch Neurol.* 2004;61:914-918.
3. Sindrup SH, Bach FW, Madsen C, Gram LF, Jensen TS. Venlafaxine versus imipramine in painful neuropathy: a randomized, controlled trial. *Neurology.* 2003;60:1284-1289.
4. Sindrup SH, Jensen TS. Pharmacologic treatment of pain in polyneuropathy. *Neurology.* 2000;55:915-920.
5. Morello CM, Leckband SG, Stoner CP, Moorhouse DF, Sahagian GA. Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain. *Arch Intern Med.* 1999;159:1931-1937.
6. Gilron I, Bailey JM, Tu D, Holden PR, Weaver DF, Houlden RL. Morphine, gabapentin, or their combination for neuropathic pain. *N Engl J Med.* 2005;352:1324-1334.
7. Rowbotham MC, Twilling L, Davies PS, Reisner L, Taylor K, Mohr D. Oral opioid therapy for chronic peripheral and central neuropathic pain. *N Engl J Med.* 2003;348:1223-1232.
8. Balantyne JC, Mao J. Opioid therapy for chronic pain. *N Engl J Med.* 2003;349:1943-1953.
9. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med.* 2003;163:2433-2445.
10. Williams LS, Jones WJ, Shen J, Robinson RL, Kroenke K. Outcomes of newly referred neurology outpatients with depression and pain. *Neurology.* 2004;63:674-677.

\*Availability pending based on controlled-substance scheduling by the DEA.

<sup>†</sup>Lidocaine patch 5%, venlafaxine, gabapentin, amitriptyline are not FDA approved for this use.

## Pharmacologic Agents Affect Pain Differently



# What's Hot in Pain Control

## New Drug Approval

A new drug, pregabalin,\* has received FDA approval for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) or with postherpetic neuralgia (PHN). Its exact mechanism is unclear but may involve modulation of the presynaptic release of excitatory neurotransmitters. Efficacy has been demonstrated in three randomized double-blind placebo-controlled clinical trials of pregabalin in DPN, and three in PHN. The six trials involved over 9,000 patients and lasted up to 12 weeks. Dosages of 300 and 600 mg, divided into two or three daily doses were efficacious at reducing pain. Onset of pain relief was rapid, occurring in the first week of treatment for many patients. There was a parallel reduction in sleep interference. The most common side effects compared with placebo were dizziness, somnolence, peripheral edema, dry mouth, blurred vision, weight gain, and attention/concentration difficulties. Discontinuation rates due to side effects were between 9% and 12% with pregabalin compared with 3% to 5% with placebo.

## FROM RECENT MEETINGS

### Low Back Pain

- **Botulinum toxin**† has been used off-label for the treatment of a variety of pain syndromes, including migraine and arthritic pain, and most recently, low back pain.
  - A recent report indicates the value of botulinum toxin A injected into paraspinal muscles for chronic low back pain (LBP).
  - Fifty-six patients (54%) derived benefit (at 3 weeks and 2 months) after first treatment at Yale University School of Medicine and Walter Reed Medical Center.
  - Initial responders continued to respond (90%) to subsequent botulinum A treatment of paraspinal muscles.
  - Side effects were transient and uncommon.

[Treatment of Refractory Low Back Pain With Botulinum Toxin A: A Prospective 14-Month Study. AAPM Abstract 107]

- Botulinum toxin also may be efficacious for treatment of persistent LBP even in postsurgical patients, according to a retrospective study of 24 patients with persistent LBP (>1 year) who had failed surgery and various other treatment modalities.
- Most patients were treated with IM injections into the lumbar paravertebral muscles (200 units on their symptomatic side and 100 units on the less symptomatic side).
- Pain relief continued for patients who received IM botulinum A at 3-month intervals. There were no significant side effects.

[Botulinum Toxin Type A for Failed Back Syndrome. APS Poster 725.]

### Osteoarthritis

- Studies presented new safety and tolerability data for **oxymorphone extended release (ER)**† in chronic pain control, focusing on treatment of moderate to severe osteoarthritis (OA) and other pain states.
  - Slow titration of the extended-release formulation minimized adverse effects in opioid-naïve patients, according to an open-label study of 61 patients at Altoona Arthritis and Osteoporosis Center. Vomiting occurred in 3.3% of patients, a significant reduction in rate. The most common side effect was constipation in 30% of patients, a percentage typically associated with opioid treatment.

Patients were on average 60 years of age, with osteoarthritis pain in a variety of sites and an average pain intensity score of 6.2 on a 0-10 increasing pain scale. The initial dose of oxymorphone was 5 mg q12h. After 2 days, the dose was increased gradually over 31 days until the patient's pain intensity score was reduced to 4 or less. Successful titration to a stable daily dose (average 24.4 mg) was possible for 70.5% of patients. For most of these patients (56%), titration required ≤2 weeks.

[Effective Titration With Oxymorphone Extended Release for Opioid-Naïve Patients With Moderate to Severe Pain From Osteoarthritis. AAPM Abstract 161]

- With the recent warnings about the potential dangers of chronic use of oral pain medications, investigators are finding alternative treatment options for chronic pain conditions without compromising efficacy.
  - Analysis of clinical data comparing the topical analgesic lidocaine patch 5%† with

oral celecoxib (200 mg) found patients with OA of the knee experienced improvement in average daily pain intensity on both medications.

- After 6 weeks of treatment, the study was halted to analyze the data in light of safety concerns regarding the COX-2 inhibitors. Of those patients treated in the lidocaine group (n = 63), 54% experienced ≥ 30% improvement in average daily pain intensity vs 62% in the celecoxib group (n = 63). Also, clinically meaningful reductions in pain were noted for both treatments at week 12.

[A Randomized, Open-Label Study Comparing the Efficacy and Safety of Lidocaine Patch 5% With Celecoxib 200 mg in Patients With Pain From Osteoarthritis of the Knee. APS poster 771]

- Patients with OA of the knee treated with a continuous low-level **heat wrap** for 8 hours reported significant benefits in pain reduction and improved flexibility, compared with placebo and acetaminophen or ibuprofen, according to clinical investigators at the Kaiser-Permanente Pain Management Center.
- The randomized, placebo-controlled, parallel design study enrolled 110 individuals with radiographic evidence of OA of the knee with moderate or greater pain. Patients treated with the heat wrap reported a pain relief score of 2.20 (± 0.17) compared to patients who took acetaminophen and reported a score of 1.58 (± 0.25). Range of motion, measured using a goniometer (180 degrees = fully extended knee), in patients treated with the heat wrap improved 17 to 21 degrees vs an 8- to 15-degree improvement in ibuprofen-treated patients.

[Therapeutic Benefits of Continuous Low-Level Heat Wrap Therapy (CLHT) for Osteoarthritis (OA) of the Knee. APS poster 781]

### Postherpetic Neuralgia

- **Lidocaine patch 5%** significantly improves quality of life for elderly patients in several pain settings with minimal risk of systemic side effects, so it can be used alone or in combination with anticonvulsants, antidepressants, and opioids.
- Geriatric patients with different types of neuropathic pain have significant improvement in sleep and other quality-of-life domains after treatment with the lidocaine patch 5%, according to data pooled from three prospective open-label trials.

Investigators documented the results in 286 patients with different types of neuropathic pain, including but not limited to postherpetic neuralgia. The patients were an average of 76.9 years of age, and had various types of neuropathic pain, including postherpetic neuralgia, diabetic polyneuropathy,

*Continued on page 11*

## For more information, log on to

**21st Annual Meeting of the American Academy of Pain Medicine (AAPM)**

Palm Springs, CA  
February 23–27, 2005  
www.painmed.org

**24th Annual Scientific Meeting of the American Pain Society (APS)**

Boston, MA  
March 30–April 2, 2005  
www.ampainsoc.org

## Arthritis and the COX-2 Conundrum:

*Continued from page 3*

preparations of hyaluronan currently available. Some of these have been shown in clinical trials to be as effective as oral NSAIDs for pain relief in OA and also of equal or greater effectiveness than intra-articular glucocorticoids. The onset of pain relief is slower than with glucocorticoids, but the effects may last considerably longer.

### Topical Therapy

Topical preparations applied to the joint are yet another approach to pain management in OA. Capsaicin, the alkaloid responsible for spiciness in chili peppers, has been used for a long time for the management of arthritis pain. It has been the subject of renewed interest because its mechanism of action is only now becoming understood. Capsaicin acts via a vanilloid receptor and depletes substance P in sensory neurons. However, there is conflicting clinical evidence for its efficacy. Burning sensations and skin irritation are side effects in some patients.

A more recently developed form of topical analgesia of OA is a transdermal patch containing lidocaine 5%. This means of delivery provides analgesia without any loss of sensation or numbness. Originally developed for use in postherpetic neuralgia, the lidocaine patch 5% has been shown to be efficacious in other forms of pain, including OA. In a recent head-to-head study of a lidocaine patch vs celecoxib, 54% of patients using the patch experienced a  $\geq 30\%$  improvement in average daily pain intensity compared with 62% of those receiving oral celecoxib.<sup>3</sup> [See page 8.]

Topical NSAIDs have been used for decades for the treatment of painful musculoskeletal conditions. However, a recent meta-analysis that examined data for OA patients showed that topical preparations of salicylate, diclofenac, and other NSAIDs were less effective than oral NSAIDs. Furthermore, after week 2 of the study, there was no statistically significant difference between topical NSAIDs and placebo in pain scores.<sup>4</sup>

### Non-NSAID Pharmaceutical Therapy

The use of opioid therapy in the treatment of pain in OA is becoming increasingly accepted and would also be suitable for our patient. Although a considerable stigma has been previously associated with the use of opioids for noncancer pain, the treatment can be highly effective for moderate-to-severe pain that requires continuous treatment. [An Opioid Analgesia Tool Kit from the National Initiative on Pain Control is available at [painEDU.org](http://painEDU.org) with downloadable tools that will help you to bring pain relief to patients, while protecting your patients and your practice. See page 12 for further details on the free CD-ROM for your use.]

The risks of addiction in patients prescribed opioids for pain control is extremely low for those who have neither a history of drug addiction nor premorbid psychopathology. Physical dependence on opioids is a predictable aspect of their pharmacology and is a quite separate phenomenon from drug addiction or drug abuse. Physical dependence is managed by dose tapering to discontinue the drug. Likewise, the fear of opioid tolerance—at least tolerance to their analgesic effects—is largely unfounded and is based largely on experience of patients with progressive diseases in which loss of efficacy is due to a worsening of the pain condition, and not to tolerance.<sup>5</sup>

Advantages of opioids include the ability to titrate doses over a wide range, and a well-characterized safety profile. Many are available in controlled-, extended-, or sustained-release forms (Table), which are of particular benefit for the treat-

ment of moderate-to-severe arthritis pain, which can be difficult to treat with prn dosing because of nighttime pain. Although opioids are available in a wide range of doses, it is important to keep to the recommended starting doses, including any dose reduction needed in patients with renal or hepatic impairment.

A recent study of oxymorphone demonstrated that slow titration of the extended-release formulation minimizes adverse effects for safety and effectiveness in older patients like Donald with chronic OA pain of the hip or knee.<sup>6</sup> Typical opioid side effects were reduced, with the exception of constipation, which can be appropriately managed using laxatives. [See page 8.]

Several long-acting opioids have been shown to be efficacious for the treatment of OA pain. Controlled-release formulations of oxycodone, hydromorphone, and morphine sulfate also have been shown to be effective at reducing pain in OA of the hip or knee. Transdermal fentanyl, worn as a self-adhesive patch for up to 72 hours, provides a non-oral route of administration, with the advantage of convenient dosing. Tramadol is considered to be opioid-like because it is a weak  $\mu$  opioid agonist, although it also functions as weak inhibitor of norepinephrine and serotonin uptake.

**Lidocaine patch 5%, and salicylate are not FDA approved for this use.**

### References

1. Food and Drug Administration Talk Paper. FDA issues public health advisory recommending limited use of cox-2 inhibitors. T04-61. December 23, 2004. Available at: <http://www.fda.gov/bbs/topics/ANSWERS/2004/ANS01336.html>. Accessed June 1, 2005.
2. Almost lost in FDA hearings, naproxen gets thumbs up. Available at: <http://healthfinder.gov/news/newsstory.asp?docID=524201>. Accessed June 1, 2005.
3. Galer B, Kivitz A, Fairfax M, Oleka N, Gammaitoni A. A randomized, open-label study comparing the efficacy and safety of lidocaine patch 5% with celecoxib 200 mg in patients with pain from osteoarthritis of the knee. Presented at the American Pain Society, Boston, Mass. March 30-April 2, 2005. Poster 771.
4. Lin J, Zhang W, Jones A, Doherty M. Efficacy of topical non-steroidal anti-inflammatory drugs in the treatment of osteoarthritis: meta-analysis of randomized controlled trials. *BMJ*. 2004;329:324-330.
5. Passik SD, Kirsh KL. Chronic pain management and substance abuse: assessing and optimizing outcomes. *ElderCare*. 2002;2:1-3.
6. Kafka S, Photivihok G, Ahdieh H, Nagle B. Effective titration with oxymorphone extended release for opioid-naive patients with moderate to severe pain from osteoarthritis. AAMP Annual Meeting Abstracts. *Pain Medicine*. 2005;6:196. Abstract 161.

## Choices of Opioids for Treating Chronic Pain

Type	Opioid
Long-acting	Hydromorphone
	Morphine
	Oxycodone
	Transdermal fentanyl patch
Opioid-like	Tramadol

## ASK THE EXPERT



**MICHAEL MOSKOWITZ, MD**  
Bay Area Pain Medical Associates  
Research consultant for Endo and a  
member of speakers bureau for  
Cephalon, Pfizer Inc, and Forrest  
Laboratories.

### Question

**What course of action do you take when a patient has broken the Opioid Patient Care Agreement?**

### Answer

Most patients requiring long-term opioid treatment are extremely unlikely to abuse opioids in the course of treatment. Such patients may commit a minor infringement at one time or other ranging from missed appointments, to seeking an opioid prescription from another doctor, or giving a single tablet to a friend or relative for relieving pain. It is important to raise the matter with them as nonjudgementally as possible without implying any form of criminality. Unsanctioned dose increases also have to be dealt with. Typically, this happens when a patient feels a need for additional medication. In such instances the patient needs to be reminded that any increase in dose must be done under medical supervision and only in response to increased pain. A treatment plan should spell out the consequences of continued infringement, such as having to pick up medication on a daily basis.

For some patients who have clear signs of addiction, continued pain management with opioids is not necessarily contraindicated. Sometimes a patient will have been free from addiction for many years and be using opioids for effective pain management, only to “fall off the wagon” at a later date. Here we request that the patient attends Narcotics Anonymous meetings on a regular basis, or we may arrange a consultation with an addiction specialist. Urinalysis, as provided for in a care plan, will indicate whether they are abusing other substances or indeed not taking their prescribed opioids. Additional harmful signs, such as a patient concealing from us a past history of drug abuse, require referral to an addiction specialist who will help devise an appropriate opioid regimen or may recommend avoiding opioids altogether.

Regrettably, there are also patients who will obtain opioids by willful deception, for example by exaggerating his or her symptoms on repeated visits. Such patients are a rare but disconcerting problem in the practice of pain management and can be

hard to detect. On such occasions it becomes necessary to remove the patient from our practice. Also, in instances where we discover a patient is engaging in clearly illegal activities, we are required to report them to the police. Examples of such activities include fraudulently calling in prescriptions under a physician's name, and selling or redistributing prescribed opioids.

### Additional Resources

1. American Academy of Pain Medicine. Long-term controlled substances therapy for chronic pain: Sample Agreement. Available at: [http://www.pain-med.org/productpub/statements/pdfs/opioid\\_consent\\_form.pdf](http://www.pain-med.org/productpub/statements/pdfs/opioid_consent_form.pdf). Accessed June 1, 2005.
2. National Initiative on Pain Control<sup>®</sup>. Opioid analgesia tool kit. A resource for managing your patients with chronic pain. FREE CD-ROM. Available at: <http://www.painedu.org>. Accessed June 1, 2005.

## Exit Strategy Guide for Discontinuation of Opioid Therapy

**The possibility of subsequent discontinuation from opioid therapy should be discussed with the patient at the time that opioid therapy is initiated.**

### Determine patient is not sufficiently responsive to opioid therapy to continue with such treatment

Suggested criteria:

- Intolerable side effects at the minimum dose that produces effective analgesia
- Reasonable attempts at opioid rotation unsuccessful
- Noncompliance with patient care agreement
- Clinically rational dose escalation without adequate analgesia
- Deterioration in physical, emotional, or social functioning attributed to opioid therapy

### Establish collaborative relationship with patient around need for discontinuation of opioid therapy

- Review exit criteria agreed upon in patient care agreement
- Clarify that exit is for patient's (not doctor's) benefit
- Clarify that exiting opioid therapy is not synonymous with abandoning pain management or abandoning patient

Patient appears to have a problem with drug addiction

Refer for addiction management or co-management

No apparent addiction problem. Patient able to cooperate with office-based taper

- Taper opioids gradually over one month
- Implement non-opioid pain management strategies, including psychosocial support, cognitive-behavioral therapies, physical therapy, non-opioid analgesics, management of insomnia, anxiety, depression

Patient unable or unwilling to cooperate with outpatient taper

- Provide sufficient opioid for one-month taper or maintenance until admission
- Refer to inpatient program or comprehensive outpatient program, or similar services as available



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 speakers bureau member for Purdue  
 Pharma L. P. and Pfizer Inc.

## Question

### How do you determine treatment success in chronic pain?

## Answer

We determine treatment efficacy from seven perspectives, most of which can be reviewed in a standard office visit.

**FIRST**, making progress toward achieving the patient's personal goals. Patients may want to become able to:

- Tolerate air travel
- Increase their walking endurance
- Concentrate well enough to read a novel
- Play more with children or grandchildren

Patients develop three to five goals with us that are specific and realistic. As goals are achieved, we develop new ones.

**SECOND**, monitoring the patient's level of preoccupation with pain.

- Is the office visit focused only on pain symptoms, pain reduction, and inquiries about new procedures?
- Does the patient spontaneously discuss any nonpain concerns?

**THIRD**, improving physical, psychological, social function.

- Is the patient able to do more, be more independent, make plans to do things with others and keep to them?

**FOURTH**, obtaining an outside informant's perspective a few times per year.

- We document how a significant other or family members view the patient's functional status, pain levels, mood, and medication side effects.

**FIFTH**, assessing neurovegetative domains often impaired by chronic pain.

- Sleep quality, energy level, appetite, and libido.

**SIXTH**, tracking self-report on standardized rating forms, including

- 10-cm visual-analog scales for current pain, least and worst pain in past 2 weeks, interference of pain on activities, and mood.

Three times annually patients complete a Beck Depression Inventory, allowing us to track overall and specific depressive symptoms.

**FINALLY**, calculating acceptance.

We look for:

- More realistic expectations from treatments
- Less catastrophic conjecture during pain exacerbations
- Pacing of tasks and resumption of social activities with necessary adjustments. For example, if patients have predictable increases in evening pain, we want to see them arrange lunch or early dinners rather than give up dining out with friends they used to meet for eight-o'clock dinners.

*We look for acceptance and adaptation, not resignation.*

Beck Depression Inventory. Information available at: <http://mail.med.upenn.edu/~abeck/scales.html>

## What's Hot in Pain Control

Continued from page 8

idiopathic neuropathy, and unspecified neuropathic pain.

They found that patients reported significant improvement over baseline 2 to 3 weeks after treatment, using the Brief Pain Inventory (BPI) at baseline. Of these patients, 144 (50.3%) had at least a 30% decrease in average daily pain. The lidocaine patch 5% was associated with a significant reduction in the degree to which pain impeded sleep and other quality-of-life factors. Treatment-related adverse effects, ie, irritation, rash, burning, and erythema, were experienced in 16 patients (5.5%).

[Lidocaine Patch 5% Improves Sleep, Quality of Life, and Pain Intensity in Geriatric Patients With Neuropathic Pain: A Pooled Analysis. AAPM Abstract 163.]

## IN THE LITERATURE

### Polypharmacy Proves Effective for Chronic Neuropathic Pain

Chronic neuropathic pain states often respond to analgesics such as anticonvulsants (eg, gabapentin), opioids (eg, morphine), tricyclic and SSRI antidepressants (eg, amitriptyline, venlafaxine),<sup>1</sup> and topical agents (eg, lidocaine patch 5%). The drugs available to treat neuropathic pain have incomplete efficacy and dose-limiting adverse effects. With the exception of topical agents that have little potential for systemic interaction, these agents must be selected with other medications in mind, as well as concomitant medical conditions, to minimize the potential for drug-drug or drug-disease interactions. "Rational polypharmacy" is a term commonly used to define a systematic approach to combining various classes of agents for optimal treatment of neuropathic pain such as diabetic peripheral neuropathy or postherpetic neuralgia.

Until now, recommendations for combination therapy were based on theoretical mechanisms, rather than on controlled trials. A recent study in the *New England Journal of Medicine* gives new credence to the rationale of polypharmacy and putative mechanisms of action in treatment of painful diabetic neuropathy and postherpetic neuralgia. In this randomized, double-blind, crossover trial, patients received active placebo (lorazepam) compared with monotherapy of morphine or gabapentin, and combination therapy of gabapentin and morphine. Gabapentin and morphine combined achieved better analgesia at lower doses of each drug than either as a single agent.

Gilron I, Bailey JM, Tu D, et al. Morphine, gabapentin, or their combination for neuropathic pain. *N Engl J Med*. 2005;352:1324-1334.

\*Availability pending based on controlled substance scheduling by the DEA.

<sup>1</sup>Botulinum toxin, oxycodone ER, lidocaine patch 5% for OA, amitriptyline, venlafaxine are not FDA approved for this use.

## E-MAIL THE EXPERT

### DO YOU HAVE QUESTIONS ABOUT CHRONIC PAIN?

Please forward your questions to our knowledgeable faculty at [nipc@pps.thomson.com](mailto:nipc@pps.thomson.com) by August 15, 2005. Then read issue 2 (Fall 2005) of *Pain Management Today*® to find the responses to your most vital patient concerns. Of course, we welcome your comments and feedback as well. **Just log on!**

## NEW! NIPC Opioid Analgesia Tool Kit

The *National Initiative on Pain Control*<sup>®</sup> (NIPC<sup>®</sup>) presents the **Opioid Analgesia Tool Kit**. This CD-ROM is steered by a user-friendly treatment algorithm that guides the physician through a comprehensive compilation of practical tools and resources to better manage their patients who require opioid therapy. These tools are downloadable for use in office-based practice. The goal is to maximize treatment benefit, while minimizing the risks associated with this therapy.

To learn more, visit **PainEDU.org**.

**PainEDU.org** was awarded the “Webby Worthy” distinction from the International Academy of the Digital Arts and Sciences. The Webby Awards are distinguished in the world of Web sites, and they have received more than 4,300 submissions in the competition.



## Another Issue Coming This Year!

In addition to our two regular issues of *Pain Management Today*<sup>®</sup>, we are publishing a supplement for Winter 2005.

The focus for PCPs will be **efficacy**, **safety**, and **precautions** to improve practice-based management of chronic pain through education on:

- Distinctive biochemical properties of analgesics
- Rationale, based on sites of action and safety, for using multiple therapies
- Key safety points for pain management
- Important regulatory issues

*See the next issue of this newsletter for more information.*

## Coming Soon! NIPC DINNER DIALOGUES<sup>®</sup> SERIES

### *Opioid Analgesia: Practical Treatment of the Patient With Chronic Pain*

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B084-017	Tues. 9/27/05	Roslyn, NY	Charles Argoff, MD
B084-018	Tues. 10/04/05	Seattle, WA	Michael Moskowitz, MD
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