

FREE

CONTINUING EDUCATION LESSON



APPROVED FOR 2 CEUS

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LEARNING OBJECTIVES

Upon successful completion of this lesson, the pharmacist will be able to:

1. identify where the knowledge and skills of the community pharmacist can positively contribute to the care of patients with chronic pain;
2. take a more active role and responsibility for medication management and patient health outcomes in this population;
3. describe in practical terms the complexity of ongoing therapy for patients with chronic pain;
4. describe in general terms the symptoms, and recommend multimodal treatment options for patients with chronic low back pain and osteoarthritis.

INSTRUCTIONS

1. After carefully reading this lesson, study each question and select the one answer you believe to be correct. Circle the appropriate letter on the attached reply card or answer online at www.pharmacygateway.ca in the CE Online section, "More CCEP-Approved" area.
2. To pass this lesson, a grade of 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

ANSWERING OPTIONS

- A. For immediate results, answer online at www.pharmacygateway.ca in the CE Online section, "More CCEP-Approved" area.
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The Role of the Community Pharmacist in Chronic Pain Management

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INTRODUCTION

"Pain is inevitable, (but) misery is optional." Tim Hansel, former mountain climber turned author, coined these seven simple words while coming to terms with severe and constant pain after a climbing accident. These words succinctly summarize the desired endpoint of chronic pain (CP) management, a condition that does, indeed, represent a "mountain to climb" for those people faced with it. Yet with determination and the support of a dedicated healthcare team, including community pharmacists, these patients can surmount the challenges and live relatively full lives.

CP is typically defined as pain that does not resolve after six months. Pain research is investigating how acute pain transforms into CP. It's important to understand that, for a portion of the population, unrelenting pain signals can cause neurochemical and structural changes in central nervous system pathways.¹ These changes are often referred to as "central sensitization," or "neuronal plasticity." Evidence is growing to suggest that adequate initial pain relief, including early interventions

by health professionals, can reduce the severity of chronic pain, should it develop.

Pain can be divided into two broad subcategories. Patients with "neuropathic pain" will generally describe their symptoms using words like "burning," "tingling," "knife-like" or "stabbing." Conditions that involve neuropathic pain include fibromyalgia, postherpetic neuralgia, trigeminal neuralgia, diabetic neuropathy or possibly even some types of headaches. Antidepressants (tricyclics or serotonin-noradrenalin reuptake inhibitors [SNRIs] such as venlafaxine or duloxetine) are commonly used drug therapies, as well as the antiepileptic drugs (AEDs) (e.g., gabapentin, carbamazepine or topiramate).

Patients with "nociceptive pain" will use words like "deep" or "achy" to describe their symptoms. Nociceptive pain is the result of inflammation or pressure, found in conditions such as osteoarthritis, low back pain, bone fractures or surgical scar pain. Medications typically used to treat this type of pain include simple analgesics (e.g., acetaminophen), weak opioids, NSAIDs/COXIBs or strong opioids.

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While there is much more literature available for the community pharmacist's role in chronic disease management for conditions such as dyslipidemia and diabetes, CP management is too often overlooked. Although there are no practice guidelines for the management of CP by pharmacists, as one of the most accessible health professionals the community pharmacist is well positioned to assist with the co-management and follow-up of these patients. The pharmacist's assessment addresses not only medication use or misuse, but also monitoring for improvement in overall function, which is as important as a reduction in the pain score.

The management of CP is complex. It usually requires multiple pharmacological and non-pharmacological interventions and, as a result, ongoing monitoring. Unlike other chronic medical conditions, defined endpoints are limited. There are no analogous "blood pressure" or "cholesterol level" indices to guide decisions in CP care. It is more about managing the overall well-being of the patient, not simply their pain score.²

Soft endpoints include: improved functioning, better moods, getting outside more often, and improved medication tolerance. A well-defined algorithm for practitioners to follow, which covers all clinical situations, does not exist. Available algorithms, such as the *World Health Organization Pain Ladder*, are not used in isolation but are supplemented by evidence-based medicine and medical clinical practice guidelines. In summary, clinicians must rely on clinical experience and the response/failure of sequential (often concurrent), evidence-based interventions when managing patients with CP.

Medication management in CP is often a case of slow titration, side-effect management and medication rotation. This is often predicated by the type of pain encountered and the choice of drug therapy which in turn is determined according to biochemical or physiological reasons or clinical evidence. A drug may be selected to exploit or avoid certain side effects to enable better overall management or to achieve analgesic synergy.

This lesson introduces community pharmacists to their role in the management of chronic pain. It uses case studies to illustrate this role in the context of different types of CP; however, it does not aim to fully explore any particular type of CP. Similarly, in-depth discussions of sleep disturbance, comparative pharmacology and addiction assessment are beyond the scope of this lesson. A useful reference for comparative pharmacology is Lynch and Watson's *The Pharmacotherapy of Chronic Pain*.¹

"Pain is a more terrible lord of mankind than even death itself."

– Albert Schweitzer, 1931

CASE STUDIES

The case studies that follow depict patients who may present in community practice, and who illustrate the management of chronic pain in low back pain and osteoarthritis. They are intended for illustration purposes only, to explore how an individual pharmacist may manage a patient with a particular pain history. Clearly, however, not all patients are managed the same, and the management presented in these cases is not intended to be all-encompassing.

CASE 1: CHRONIC LOW BACK PAIN

Rose Stoick is 56 years old. She slowly became aware that her low back pain (LBP) was not resolving despite self-medication with simple analgesics, including acetaminophen. Rose cannot recall any precipitating event. She sought medical attention and ultimately underwent lumbar decompression surgery in 1994, doing reasonably well, but taking "a couple of years" to fully recover by her estimation.

In late 2004, Rose noticed a sudden onset of LBP that radiated into her right leg. She was diagnosed with spinal stenosis and underwent a second back surgery in December 2005 with good surgical results (according to her surgeon), but she continues to have pain.

Rose had rheumatic fever as a child. Rheumatic fever has an inflammatory component that may cause long term cardiac sequelae, including valve dysfunction and possible arrhythmias. It is important to consider the risk of endocarditis with procedures and the possible need for prophylactic antibiotic coverage. Rose is not currently experiencing any of these sequelae (she is asymptomatic from a cardiac point of view) but the potential for cardiac sequelae must be kept in mind.

Rose takes venlafaxine 225 mg daily and bupropion 300 mg daily for depression, as well as atorvastatin 20 mg daily for hyperlipidemia and conjugated estrogens 0.3 mg per day. She has no other medical conditions.

In July 2008 she presents with a prescription for nortriptyline 5 mg at bedtime with instruction to titrate upwards once weekly. She is unclear why the doctor gave her another antidepressant drug for her "hot-knife" back pain. You check her profile and confirm with her that she is still taking bupropion and venlafaxine. She is tapering those medications per her doctor's instructions. She feels her mood

is much better but sleeping is still an issue, which she attributes to unrelieved pain at night as well as a new back pain "flare." Ultimately the plan will be for her to completely discontinue the bupropion and use a much lower dose of venlafaxine.

A. What advice about nortriptyline would you give to Rose? What additional information can you give her about chronic LBP (CLBP)?

You reassure Rose that combinations of different medications are often used for CP management, including chronic low back pain. The nortriptyline should help her sleep and reduce her new back pain after two or three weeks, as the medication is titrated. You explain that nortriptyline must be started at low doses and gradually increased, no more than once a week, in order to achieve effectiveness without significant side effects. You ask her to watch for daytime drowsiness in particular. You offer to follow up with her to make sure she is feeling all right during this dose titration, and to help ensure she's tapering the bupropion and venlafaxine. You reassure Rose that CLBP can be managed, and encourage her to contact you or her physician should she experience any new symptoms or have any concerns.

LBP is the fifth most common reason for all physician office visits³ and about two-thirds of adults will suffer from LBP at some point in their lives.⁴ Despite adequate medication trials, this condition remains a major socioeconomic problem. If pain persists for more than 12 weeks, a provisional diagnosis of CLBP is often made. Some typical signs and symptoms ("red flags") include:⁵

- lack of response to conservative measures over a course of two to three weeks;
- back pain for more than six weeks;
- age greater than 50 years;
- pattern of pain not consistent with mechanical back pain (resulting from over-activity); progressive neurological deficit (numbness, tingling, loss of sensation), new back or leg pain or leg weakness, pain worse at night not relieved by a change in position, fever > 38 degrees C (100 degrees F), loss of bowel or bladder function (urgent physician assessment within 24 hours); and
- if rapid onset of loss of bowel or bladder function +/- neurological deficit, immediate physician assessment is required.

Non-prescription therapies also play a role in CLBP management. These include:

- continuation of routine daily activities if possible and avoidance of activities such as bending, lifting, twisting movements or prolonged sitting;

- bed rest is *not recommended* beyond a day or two, to a maximum of *four* days;
- modification of activity to slowly increase certain forms of exercise, such as low-impact aerobics, swimming and cycling;
- the use of hot or cold packs (as preferred) to decrease inflammation/pain; and
- the use of simple analgesics (i.e., ASA, ibuprofen, acetaminophen).

If a patient reports no improvement or a worsening of symptoms, or if high pain levels continue for more than a week, the pharmacist should recommend an appointment with their physician.

Rose returns to your pharmacy in early December 2008; she advises you she didn't tolerate the nortriptyline (30 mg at bedtime) well, primarily due to daytime grogginess. She made several attempts at trialing the medication but she just could not tolerate the drug, even though it did give her significant pain relief. She reminds you that she has tried amitriptyline in the past and states it was even worse.

Rose is obviously frustrated, and says she's worried this will get her down, particularly with Christmas just around the corner. She adds she doubts she'll be able to see her doctor any time soon, since she's so busy with Christmas preparations. She asks for your recommendation. You respond that there are other treatments available, and that you'll discuss them with her physician and follow up with her.

B. What other medication choices might be appropriate for Rose?

There is little evidence to demonstrate that one NSAID is superior to another, or that NSAIDs are superior to TCAs or opioids (see Table 1) for CLBP. A recent review found little data on the long-term safety of NSAIDs in CLBP.³

The reader should keep in mind Rose's good analgesic response to TCAs when considering alternate choices. She has tried simple analgesics with little benefit, she has had dose-limiting side effects from TCAs, she has a history of rheumatic fever and NSAIDs may not be the best choice given their cardiovascular risks.

Tramadol is an option, but given Rose's poor tolerance to TCAs it may be poorly tolerated as well, since a majority of tramadol's activity is the reuptake inhibition of the neurotransmitters noradrenalin and serotonin. Tramadol also functions like an opioid in that it also binds to the μ opiate receptor, albeit with weak affinity.

It is extensively metabolized to the active M1 metabolite which binds many times tighter to the μ receptor (some reports indicate

TABLE 1: Medications for Chronic Low Back Pain, Summary of Evidence

Drug	Net Benefit	Quality of Evidence	Comments
Acetaminophen	Moderate	Good	Liver function; concomitant NSAIDs
Antidepressants	Small to Moderate	Good	Only TCAs have shown to be effective for CLBP Little evidence on duloxetine or venlafaxine
Antiepileptic drugs	Small to moderate	Poor	Small trials of gabapentin and topiramate
NSAIDs	Moderate	Good	Risk of cardiovascular events Insufficient evidence benefit vs harm for celecoxib
Opioids	Moderate	Fair	Risk of abuse/addiction
Tramadol	Moderate	Fair	

Adapted from Chou and Huffman Annals Int Med 2007³

200 times tighter) than the parent compound. It is contraindicated in severe hepatic dysfunction and with renal clearance less than 30 ml/min as approximately 30 per cent is excreted as unchanged parent drug.

Half-life elimination of the tramadol is approximately six to eight hours with the M1 metabolite being seven to nine hours. These values are prolonged in the elderly and of course in hepatic and renal dysfunction.

Caution should be exercised when using tramadol in the elderly (> 75 years). Given the TCA-like effects of the drug, a conservative titration scheme should be used, with a maximum suggested dose of 300 mg per day. Very careful consideration should be undertaken when using the long acting forms of the drug in the elderly or hepatic dysfunction.

Although it has much less risk for anticholinergic side effects than the TCAs, patients may still describe problems if they have had previous tolerance issues with the TCAs. Of course, the low risk of serotonin syndrome still exists. This syndrome results from the accumulation of serotonin in the nerve synapses and may cause shakiness, irritability, sweating or possibly seizures. It usually occurs when high doses of two or more serotonergic drugs (e.g., SSRIs, certain TCAs or MAOIs) are used simultaneously or there are clearance problems associated with their use.

Gabapentin, on the other hand, may be tolerated better given Rose's history. Although gabapentin does not have strong evidence for use in CLBP, it has demonstrated pain relief activity.³

You discuss these options with Rose's physician. You both agree that improved tolerance

is the primary goal for this particular patient at this time, and decide that gabapentin should be initiated using a slow escalation. A reasonable regimen would be to start at 100 mg twice daily and escalate by 100 mg weekly using a TID dosing schedule, monitoring for sedation, cognitive ability, dizziness, weight gain and edema. Baseline renal function assessment is also advisable but not recommended on an ongoing basis.

Analgesia from gabapentin may be expected to begin at approximately 1000 – 1200 mg per day^{1,2} keeping in mind that dose-response varies between individuals.

You advise the physician that you will make weekly follow-up phone calls to monitor adverse effects, analgesic response, ataxia, cognition and overall functioning and will report back as required.

However, the doctor states he would like to see Rose first before prescribing gabapentin, even if that means waiting until after Christmas. After confirming that Rose has sufficient supplies of nortriptyline, you suggest decreasing the dose to 20 mg daily in an effort to reduce the daytime drowsiness without losing too much analgesic benefit. The physician agrees with this approach and gives you a verbal order to decrease the dose to 20 mg at bedtime for three weeks. Dosing for TCAs for most types of CP is generally initiated at 10 to 20 mg, titrated weekly. A minimal effective dose is generally 40 to 50 mg per day, with maximal dosing typically reported to be 150 mg per day.¹

Dose ranges for AEDs are more variable, but typically less than those used for epilepsy. Neither class of drug shows a good correlation

between serum level and analgesic response. The only correlate is that a serum level in the high “epilepsy therapeutic” range should provide maximal relief whereas the inverse is not necessarily true.

C. How do you provide ongoing pain care management for Rose?

You will continue your established practice of follow-up phone calls. Non-adherence to medication for chronic disease management is a significant issue for all patients. Phatak and Thomas conducted a survey of patients waiting to see outpatient pharmacists in a primary care clinic. The investigators were examining the association between patient medication beliefs and non-adherence to chronic drug therapy.⁶ Results showed little correlation between the necessity for chronic use of medications and non-adherence ($p < 0.08$) but significant concerns with respect to correlation between:

- a) patients’ specific concerns related to chronic drug therapy and non-adherence ($p < 0.001$);
- b) perceived general overuse (over-prescribing) and non-adherence ($p < 0.0001$); and
- c) perceived general harm related to medications and non-adherence ($p < 0.001$).

Medication beliefs alone accounted for 22.4 per cent of the non-adherence variation.

This survey corroborates an earlier study by R. Horne and J. Weinman.⁷ Most patients believed their medication was necessary for the treatment of their condition but one-third expressed strong concerns based on beliefs about the dangers of dependence or long-term effects.

The Visual Analogue Scale (VAS) is frequently used as a standardized pain assessment tool. It is a numeric scale which is ranked on a range of 0 to 10 with 0 representing “no pain” and 10 representing “worst imaginable pain”. A one- to three-point drop in the VAS is considered a significant and well-accepted response. Practitioners are cautioned against using the VAS for patients whose descriptions of pain are not linear or for those who have difficulty using a numerical rank (a non-graduated line or verbal expression may be more appropriate).

CASE 2: OSTEOARTHRITIS

Jack Hobbler is a 58-year-old retired executive. He has multiple medical problems in addition to struggling with osteoarthritis (OA) for many years: Type II diabetes mellitus, declining renal function, hypertension and essential tremor. He is overweight and has a background issue of myofascial pain. His major pain prob-

lem, however, is his bilateral knee OA. For mobility reasons, Jack now lives in a split bungalow that has a large yard for his two small dogs. Since his retirement, he leads quite a sedentary lifestyle. His current list of medications includes:

- Venlafaxine 150 mg a.m. / 75 mg p.m.
- Insulin Lispro 7 u TID
- Insulin glargine 10 u HS
- Allopurinol 100 mg daily
- Furosemide 20 mg BID
- Omeprazole 20 mg daily
- ASA 81 mg daily
- Propranolol 40 mg daily
- Lisinopril 10 mg daily
- Rosuvastatin 20 mg daily

Jack also takes multivitamins and occasionally receives intra-articular injections of hyaluronate.

OA, particularly of the knee, is the most common form of arthritis in western developed countries. It is a chronic condition that typically worsens with weight-bearing activity. It is characterized by joint cartilage loss and replacement by new bone formation. Often it is accompanied by morning stiffness and, with continued inactivity, immobility of the affected joint. Knee OA is as disabling as cardiac disease and is more common than all other medical conditions in the elderly.⁸ A recent report from the World Health Organization predicts it will become the fourth most important global cause of disability in women and the eighth most important cause in men. Clearly this has an immense impact on health, economics and social costs. The predominant risk factors are age, obesity, previous trauma (particularly in men), and activities requiring repeated knee bends.

Jack comes to your pharmacy in April 2008 and asks about glucosamine for his knees or if there is something else he could consider. You see this as a good opportunity to discuss an overall pain management plan for him. You explain there are several aspects to managing his OA and medications are just one component of the total care. Other modalities include non-prescription options, including non-prescription drugs, physical medicine approaches and education.

An overarching goal of CP management, regardless of type, is that global improvement in function is as important as an absolute improvement in pain score.^{1,2} Often a significant increase in analgesia (decrease on the VAS) is accompanied by dose-limiting side effects that impact quality of life. Gradual dose adjustment, making only one change at a time and a “start-low-go-slow” approach as a means to minimize side effects and optimize analgesia, is the usual method. It is important to

inform Jack that a reduction of one to three points on the VAS with the use of pharmaceuticals alone is a well-accepted and clinically realistic goal. Clinical trials demonstrate similar results using an 11-point scale.⁹ In other words, medications are unlikely to completely “take the pain away,” but they will make it more “tolerable” or “bearable.”² Lifestyle modification and chronic disease management programs are equally important components of the management of pain in OA and CP in general.

A. What are the non-prescription options you might suggest?

This is an opportunity to discuss effective self-management options for Jack’s OA. You reinforce that some of these would also be beneficial for his diabetes and hypertension, in addition to overall well-being. Glucosamine +/- chondroitin are slow-acting drugs requiring at least a three-month trial, but have favourable side effect profiles. There is some controversy in the literature, with glucosamine +/- chondroitin showing benefit in meta-analysis⁸ but not individual single studies. Glucosamine is possibly more effective in moderately advanced disease as opposed to mild cases,¹⁰ although other references state the opposite. In addition, a recent meta-analysis of chondroitin has demonstrated little overall benefit.¹¹

One aspect of OA that not all patients appreciate is that medication is just one part of the overall plan for pain management. Non-pharmacologic therapies play a significant role and in some cases may be effective on their own (though most often treatment is multimodal). Principal among these non-pharmacologic options, which the community pharmacist may suggest, are education, exercise programs, weight reduction and appropriate footwear. Encourage patients to contact self-management programs or physical medicine specialists such as physiotherapists or kinesiologists for joint protection and energy conservation. An occupational therapist may also be appropriate for advice on assistive devices or daily activity assessment. Jack thanks you for your time and says he will talk to his physician about exercising. He decides not to try glucosamine for now.

Jack returns to your pharmacy in June to pick up some refills. He remarks that he and his family doctor agreed on an exercise plan and he has lost about five pounds, but now he would like your help choosing an analgesic. Further questioning reveals his pain flares up a bit during his walks and then settles down with rest. He denies having any sharp pains but describes a deep “achy” type of pain. You

explain that acetaminophen is still considered first-line therapy for OA, as it is the least likely to cause side effects and may well be efficacious enough, even for the long term.⁸ You also remind Jack that several weeks at full dose are required to establish efficacy. Given there is no cure for OA, treatment is primarily directed at pain reduction and improved functionality (improved joint function). Table 2 indicates recommended treatment options for OA pain reduction.

About six weeks later Jack returns to your pharmacy with a prescription for celecoxib 100 mg BID. He has lost a further 10 pounds, feels great, but his knees are really starting to bother him and the acetaminophen just doesn't seem to be working very well, even at the maximum dose of eight 500 mg tablets per day.

TABLE 2: Osteoarthritis – Evidence-Based Recommendation, Selected Therapies

Intervention	Level of Evidence	Strength
Acetaminophen	1B	A
Opioid analgesics	1B	B
Tramadol	1B	B
Conventional NSAIDs	1A	A
COXIBs	1B	A
Antidepressants	1B	B
Topical NSAIDs	1A	A
Topical capsaicin	1A	A
Glucosamine	1A	A
Chondroitin	1A	A
IA hyaluronate	1B	B
IA corticosteroids	1B	A
Education	1A	A
Exercise	1B	A
Telephone follow-up	1B	B
Weight loss	1B	B
Insoles	1B	B
Orthotic devices	1B	B

Adapted from Jordan K et al EULAR Knee Recommendations⁸

Alpha-numeric rankings for "Levels of Evidence":

Level 1 evidence indicates the evidence was obtained through randomized controlled trials (RCTs) and / or meta-analyses and there was agreement on outcome. The alphabetical qualifier indicates the quantity or size of those clinical trials; 1A evidence would indicate a study outcome with several RCTs while 1B evidence may indicate only 1 RCT, hence 1A evidence has a higher level of confidence. "Strength" refers to other factors such as side effect profile, magnitude of the effect, economics, etc.

Caution should be exercised when NSAIDs (including COXIBs) are prescribed in patients with renal function of < 60 ml/min.¹³ All NSAIDs/COXIBs may raise blood pressure (systolic 3-7 mm Hg) in normotensive as well as hypertensive individuals. This may be further complicated in a patient who might be volume-depleted (e.g., as a result of taking diuretics). The reasoning is due to decreased production of vasodilating prostaglandins in the kidney tissue, whose synthesis is compromised by these medications, thus further compromising renal function. As a result, the lowest effective dose of the NSAID/COXIB should be used. If the decision is made to start Jack on an NSAID, full gastroprotection should be offered, including scheduled doses of a proton pump inhibitor. Increasing Jack's omeprazole dose to 20 mg BID should also be considered, as he does have GERD and he is on low-dose ASA.

Jack is considered to be at increased cardiovascular risk given his diabetes, hypertension and excess weight. The cardiovascular risk associated with NSAIDs/COXIBs is thought to be due to a relative imbalance in promotion (thromboxane) versus inhibition (prostacyclin) of platelet aggregation, leading to an imbalance in favour of thrombosis. It is also thought that prostacyclin may inhibit the formation of atherosclerosis. NSAIDs vary in their selectivity for cyclooxygenase inhibition and therefore demonstrate a varying likelihood to cause platelet aggregation imbalances, hypertension and renal perfusion. However, mounting evidence suggests that non-selective NSAIDs offer little advantage in cardiovascular risk compared to COXIBs.¹⁴

You are a little concerned about Jack's renal function and phone his family doctor to discuss the appropriateness of the celecoxib prescription. He is about to leave on a well-deserved vacation, and won't have time to order lab tests until he is back. Together you decide the best interim plan is to use a topical NSAID, diclofenac 5% gel applied twice daily, refill x 3. You dispense the topical diclofenac and make arrangements to call Jack in a week to discuss efficacy and side effects.

In September Jack informs you his diclofenac gel doesn't seem to be working as well. He asks you if it is possible for "the stuff to go bad." You reply that it is more likely the topical preparation is starting to lose its effectiveness.¹⁵ He questions whether the celecoxib would have been better. You call his family doctor. Jack's blood work is back and his creatinine clearance and glomerular filtration rate (GFR) have been slowly declining (calculated creatinine clearance is now 57 ml/min). The ensuing discussion revolves around the pros and cons

of NSAIDs and eventually the decision is made to abandon anti-inflammatories and proceed to mild opioids. Jack's physician thanks you for your help and provides a prescription for acetaminophen 300 mg/caffeine 15 mg/codeine 30 mg 1 or 2 tablets q4h prn, supply 100. Note that opioids are not recommended as maintenance therapy of OA, but may be considered appropriate therapy in well chosen circumstances.

B. What do you discuss with Jack regarding his new prescription and the issues of dependence and addiction?

The risk of addiction is a concern when using opioids for chronic non-cancer pain management, although genuine addiction among pain patients is relatively uncommon. Assessment of addiction in the CP patient is complex. Healthcare providers' fears about the risks of addiction complicate this further, often leading to under-treatment.

You explain to Jack that it is important to distinguish between dependence and addiction. **Dependence** is expected to occur when treatment with an opioid continues over a long period of time. It is often defined as a physiological state in which the patient can experience withdrawal symptoms if the drug is abruptly ceased, the dose is rapidly decreased or an antagonist is administered. For example, patients treated with short-acting antidepressants (e.g., venlafaxine or an SSRI) often experience withdrawal symptoms due to dependence. This of course also happens with opioids.

Addiction is a chronic neurobiological disease with environmental and psychosocial factors^{1,16} that influence behaviours, including:

- impaired **control** over drug use;
- **compulsive** use;
- **continued** use despite harm; and
- **craving**.

These factors are separate and distinct from dependence. The diagnosis of addiction is made by the observation of a pattern of behaviour over time. Such aberrant behaviours may include: disputes about analgesics, using illicit drugs to manage pain, using another person's analgesics, giving prescribed analgesics to another person, tampering with analgesic delivery systems, obtaining prescriptions from multiple sources and, of course, using multiple pharmacies.

A recently identified condition that complicates pain management is "pseudoaddiction." This may occur when pain is poorly controlled and the patient attempts to obtain added analgesia. It is easy to see how this may be viewed as drug-seeking behaviour. Only

when pain management improves and behaviours resolve, can it be distinguished from true addiction. Patients who are “pseudoaddicts” may argue over their medications but still try to actively manage their pain, while the addicted person may be very passive in this regard.

Tolerance is a physiological event where diminished response to the drug occurs over time. Often this will result in the need for adjustments to the medication regime.

Jack returns to your pharmacy in October with a prescription for controlled-release codeine 50 mg twice daily, Mitte: 100. You ask him how his pain is and he seems somewhat defensive. He says the codeine isn't working very well and his doctor gave him something “stronger.” You explain it is still codeine but in a long-acting form that should give him better pain control over the course of the day.

He returns in six weeks, sooner than expected, with a new prescription for controlled-release codeine at a dose of 50 mg TID. He is a little more abrupt than his usual self, he tells you what the dose is and that he “needs” it. You caution him about overuse of the codeine and to keep track of how much he is actually using. He asks about addiction and you allay his fears by stating this is unlikely in a CP patient. He does mention he is aware of his increased use but is trying to manage his pain. You reinforce the idea of keeping a pain diary in order to track his “pain journey.”

Jack returns to your pharmacy in January 2009. He is now taking controlled-release codeine 100 mg twice daily and is not as defensive and not using as many acetaminophen/caffeine/codeine tablets. He remarks he is staying on schedule and his pain control is better. He admits to trying controlled-release codeine 200 mg twice daily on his own initiative but he had more side effects and it just didn't seem to last any longer. He is wondering if there is a different medication he could try.

C. What other options exist for Jack?

What could have explained the change in analgesic response and side effect profile? Perhaps Jack was under-dosed: he may have become more focused on his pain by the frequent use of the acetaminophen/caffeine/codeine tablets; he may have been experiencing “end of dose failure” where the 200 mg dose of controlled-release codeine was too much but didn't last long enough; a 100 mg q8h regimen may have been needed to address his pain needs. It is worthwhile remembering the maximum analgesic ceiling dose for codeine has been reported

TABLE 3: Opioids Commonly Used in Chronic Pain Management

Drug	Dose equivalent to morphine	IM:PO potency
Morphine	20 – 30 mg	1:3
Oxycodone	10 – 15 mg	
Hydromorphone	4 – 6 mg	1:3 -5
Codeine	200 mg	1: 1.5
Fentanyl	Consult conversion table in the CPS	

Adapted from Lynch and Watson¹

Note: This table is for information purposes only for the management of chronic pain. Doses used in acute pain are significantly different and an appropriate reference should be consulted.

to be 600 to 800 mg per day.

He is already using intra-articular hyaluronate and has used intra-articular corticosteroids in the past. He doesn't care for the injections as they are invasive and he can't exercise for a couple of days after. He finds their effect is diminishing.

Jack is concerned about the risks of addiction and dependence and also voiced concerns over side-effect management of the codeine (e.g., constipation). Tramadol may be a viable option, in spite of mixed reports of efficacy ranked from high levels of evidence from the EULAR (European League Against Rheumatism) guidelines⁸ to modest activity such as that ranked by a recent Cochrane Collaboration review.¹⁷ It is a synthetic centrally-acting analgesic that mildly inhibits the reuptake of serotonin and norepinephrine, much like the activity of TCAs. Its active M1 metabolite displays high opiate receptor binding affinity but relatively mild opiate agonist potency. The drug has been in clinical use in Europe for more than 30 years and surveillance data has indicated it is of low addiction risk potential.

The availability of tramadol in Canada represents a useful addition to the choices available to treat chronic pain. In the case of Jack it represents an alternative where an intermediate step can now be taken before moving to strong opioids. Many healthcare providers do not fully understand the optimal use of strong opioids and if they are used, often it is inappropriately. A clear advantage of tramadol is the low risk of dependence while exerting some mild opioid activity; it also has mild neuropathic modifier (TCA-like) properties. These two pharmacological mechanisms of action are central to its activity in CP. Tramadol is considered to be equipotent to codeine;¹ for example, one tramadol 37.5 mg/acetaminophen 325 mg tablet is considered to be comparable in potency to an acetaminophen 300 mg/caffeine 15 mg/

codeine 30 mg tablet.

You phone Jack's doctor about making the switch from controlled-release codeine to tramadol. He agrees this is an approach worth considering. He prescribes tramadol 100 mg daily, titrating upwards every four to five days to a maximum dose of 300 mg per day. You counsel Jack on this new medication, reminding him of the “start-low-go-slow” approach, and give instructions for tapering the controlled-release codeine.

Initially Jack tolerates the tramadol well but 12 days after filling the prescription he calls you because he feels a little dizzy, tired and just not himself. You confirm he is now taking tramadol 300 mg daily. You believe Jack escalated his dose too rapidly in an attempt to gain better pain control. He is still taking the controlled-release codeine 100 mg BID, ignoring your tapering advice. He tells you he is going to quit taking “this stuff” and just “suck it up” and use the codeine. You advise him that it is likely just a dosing issue and you advise him to drop back to tramadol 200 mg per day and increase his dose no more often than once weekly. You remind Jack that a continued taper in the controlled-release codeine is warranted and he should decrease it to 50 mg twice daily. He agrees to continue with the tramadol using this approach. You document this discussion and the plan on his record of care.

You call Jack in two weeks. He is about to increase to tramadol 300 mg per day as directed. You remind him that he doesn't have to increase the tramadol to 300 mg if his pain is well-controlled at 200 mg per day. He remarks that overall he does feel better even though he is on a lower dose. He is also taking plain acetaminophen at the lower recommended dose of 2000 mg per day. You remind him again the goal is improved functionality and not just better pain scores. Jack also feels his myofascial pain is better. You tell him you will follow up with him again in a few weeks.

SUMMARY

Chronic pain is a complex disease to treat. Often it requires multiple medication changes and side-effect management with ongoing follow-up and monitoring. Non-adherence is a significant problem in chronic disease management and certainly not restricted to medications only; the patient must become a partner in the management of their pain.

Medications are typically able to achieve pain reductions representing a one- to three-point drop on the VAS; larger responses occur but are uncommon. Full pain management almost invariably requires multi-modal treatment, which is truly interdisciplinary. The final common endpoint, regardless of the modality (be it medication, physical therapy, education or counselling sessions) is an improvement in overall functioning. The community pharmacist is clearly well-positioned to have a favourable impact on the care of these patients.

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QUESTIONS - Answer online at pharmacygateway.ca

1. **An over arching goal of chronic pain management is:**
 - a) improvement by six months
 - b) reduction in pain scores
 - c) improved functionality
 - d) improved medication management
 - e) b and c are equally important
2. **Which would not be considered to be a risk factor for the development of osteoarthritis (OA):**
 - a) participation in a range of physical activities
 - b) obesity
 - c) advancing age
 - d) prior trauma
3. **Tricyclic antidepressants (TCAs) are considered drugs of choice for CLBP. Which of the following would not be considered a dose-limiting factor?**
 - a) pro-arrhythmia effects
 - b) urinary retention
 - c) weight loss
 - d) weight gain
4. **The preferred alternative to amitriptyline due to daytime sedation, and which would still be effective for sleep induction would be?**
 - a) nortriptyline
 - b) fluoxetine
 - c) imipramine
 - d) venlafaxine
5. **With respect to Case 2 (OA), if the tramadol does not provide adequate analgesia and his pain is not neuropathic a preferred choice for Jack's OA would be:**
 - a) venlafaxine
 - b) a conventional NSAID
 - c) a strong opioid
 - d) weekly corticosteroid intraarticular injections
6. **Which of the following is not considered to be a "red flag" for low back pain?**
 - a) lack of response to a first line neuro-pathic modifier
 - b) pain worse at night, unrelieved by position change
 - c) pain attributable to overactivity
 - d) symptoms of leg weakness
7. **Which medication or pharmacological class would not be considered as first line therapy for chronic low back pain?**
 - a) antidepressants
 - b) NSAIDs
 - c) acetaminophen
 - d) antiepileptic drugs
8. **Which of the following is not a goal of a "start-low-go-slow" approach?**
 - a) maximize analgesia
 - b) achieve the proper drug serum level
 - c) minimize side effects
 - d) allow the patient to self manage their medications within set boundaries
9. **In reference to Case 1 (CLBP), Rose Stoick experienced analgesic response but dose-limiting side effects from TCAs. If she were to be prescribed tramadol, and were to experience significant benefit from it, the most likely reason for this would be:**
 - a) Tramadol also has opiate-like effects equivalent to codeine.
 - b) Her body has no tolerance to tramadol.
 - c) Tramadol has dual transmitter reuptake inhibition.
 - d) It is more potent than the TCAs.
10. **According to the Phatak and Thomas study, there is a correlation between medication beliefs and adherence. Which of the following statements is FALSE?**
 - a) There is a positive correlation between patient concerns about chronic drug therapy and non-adherence.
 - b) There is a positive correlation between perceived over-prescribing and non-adherence.
 - c) There is a positive correlation between general harm with medications and non-adherence.
 - d) There is a high correlation between the need for chronic use of medications and non-adherence.
11. **The Visual Analog Scale (VAS) is a common tool used in chronic pain management. The following are limitations to its use EXCEPT:**
 - a) Pain can be non-linear.
 - b) Some patients have difficulty in assign-

ing numerical ranks.

- c) Global functionality is not considered.
- d) The VAS is a standard tool.

12. Opioid conversion tables are not always an accurate way to convert from one opiate analgesic to another because most tables were based on acute pain or single dose studies, not chronic pain. A safe method to convert to another opioid is to assume there will be a greater response with the second opioid and reduce the target dose by 25%. If we assume morphine is 10 times as potent as codeine, what would be the approximate dose of morphine to suggest for a patient currently on 400 mg per day of extended release codeine (The resulting dose can then be titrated up if analgesia is sub-optimal).

- a) 15 mg TID extended release morphine
- b) 15 mg BID extended release morphine
- c) 10 mg QID extended release morphine
- d) 15 mg QID extended release morphine

13. With reference to Case 2 (OA), Jack was not given celecoxib or a non-selective NSAID due to his declining renal function; all of the following may exacerbate his renal dysfunction EXCEPT:

- a) diuretics
- b) antihypertensives
- c) low-dose ASA
- d) diabetes

14. Tramadol is a mixed "function" analgesic with high affinity but low potency at the mu opioid receptor. It is also possesses TCA-like activity. Caution must be exercised if it will be added to existing high-dose opioid therapy. With specific reference to

tramadol, why is this so?

- a) added sedation
- b) hallucinations
- c) drug interactions
- d) graded loss of analgesia

15. Addiction is a chronic neurobiological disease with environmental and psychological factors that culminate in that person's particular set of behaviours. "Pseudoaddiction" is a phenomenon where a patient's pain is poorly controlled and attempts are made by that person to gain pain control. It has been stated there is one defining condition that separates true addiction from pseudoaddiction. That condition is:

- a) The use of illegal drugs to supplement analgesia.
- b) When pain management improves and aberrant behaviours resolve.
- c) Obtaining pharmaceuticals from several different health care providers.
- d) The withdrawal symptoms are the key diagnostic indicator.

16. The diagnosis of addiction may be considered if:

- a) The patient increases their dose without permission.
- b) The patient continues to use the medication in spite of known harm to themselves.
- c) A pattern of aberrant behaviours is observed over the course of time in the context of increasing pain.
- d) The patient is known to have filled their prescriptions at many different pharmacies.

17. Non-pharmacological therapies for chronic disease are recognized evidence-based options for patient care. Of the possible answers listed below, which is the most correct with reference to recognized non-pharmacological

therapies for osteoarthritis (OA)?

- a) targeted weight loss
- b) athletic footwear
- c) telephone follow-up
- d) a and c
- e) a, b and c

18. Antiepileptic drugs (AEDs) are frequently used for management of several types of chronic (neuropathic) pain. They are often described as drugs with narrow "therapeutic windows." Lab tests to determine serum levels of AEDs may be performed for all these reasons except:

- a) to "monitor" organ function
- b) to ensure a defined therapeutic serum level is met
- c) to monitor compliance
- d) to enhance toxicity monitoring

19. Skin rashes secondary to certain classes of antiepileptic drugs (AEDs) are a common side effect. Consider a patient who has been using topiramate for CLBP and subsequently develops a severe skin reaction. A reasonable alternative in this patient would be:

- a) oxcarbazepine
- b) lamotrigine
- c) carbamazepine
- d) desipramine

20. The following phrases best describe chronic pain EXCEPT:

- a) Interdisciplinary team management is a highly recommended approach.
- b) There is unresolved pain after six months.
- c) Best treatment approach is aggressive single "modality" therapy.
- d) The general population has a very low awareness of this medical condition.

FACULTY: The Role of the Community Pharmacist in Chronic Pain Management

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Reviewers

All lessons are reviewed by pharmacists for accuracy, currency and relevance to current pharmacy practice.

Continuing Education Project Manager

Sheila McGovern, Toronto, Ont.

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