

## SELF-ASSESSMENT MODULE

### Pain Management

### LAFP Winter Conference

2008

#### General Principles

1. You decide to use a pain rating scale to help guide the management of a 77-year-old female with peripheral neuropathy who has daily pain.

True statements regarding these scales include which of the following? (Mark all that are true.)

- A. They are simple and easy to administer
- B. They eliminate embellishment of pain
- C. The emotional state of the patient can influence the rating
- D. There are valid scales which are useful in children

Pain rating scales are used by many physicians to measure intensity of pain and monitor the effect of therapy. (C level recommendation, evidence level II) They can be administered in a matter of minutes and are easy to score. These scales can be adapted for any age group by substituting words and/or pictures. Most children understand that 10 is greater than 2 and can use the simple 1-10 scale.

There are four scales in wide use: numeric rating scales, verbal rating scales, visual analog scales, and pain drawings. Some clinicians use pain diaries to further enhance the rating's accuracy and provide information on function. One drawback is that the scales allow for embellishment and can be skewed one direction or the other by someone with little pain experience (Evidence level III). A teenager who is naive to pain might rate the pain of a sore throat as a 10, or a patient seeking sympathy or additional treatment might overrate the amount of pain he or she is having. Emotions affect the pain experience and can also affect the rating. While there is some controversy about how accurate these scales are, most clinicians have learned to use them for assessment and management of pain.

---

2. A new patient comes to your office for evaluation of pain. The patient history should include which of the following? (Mark all that are true.)

- A. Identification of possible pain generators
- B. A worker's compensation and litigation history
- C. A history of the onset and progression of the pain
- D. A complete medication history
- E. A substance abuse history

In the evaluation of pain, the history may be more valuable than the physical examination. An important goal of the encounter is to identify the pain generator when possible, and the history may be the most illuminating part of the evaluation in this regard (C level recommendation). Often the specific pain generator cannot be identified. History taking requires very active listening, with interplay between what the patient is saying and the physician's interpretation and clarification.

Obtaining a history of the onset and progression of the pain is of great importance. It can tell the physician whether this is an acute process and if immediate action is needed (C level recommendation). It also provides clues as to the amount of additional history that will be needed to sort out previous treatment successes and failures. A history of legal action related to pain, for example, is associated with a worse prognosis.

The medication history is a very important part of the initial evaluation. Rather than just a list of medications the patient is taking, it should include a discussion of efficacy, tolerability, and economics (C level recommendation). It might also provide some idea of the patient's attitudes toward medicines and expectations for efficacy. A history of substance abuse must be elicited because it has important implications in the treatment plan and the need for safeguards

---

3. Goals for treatment of chronic pain include which of the following? (Mark all that are true.)

- A. A return to full-time employment status
- B. Improved physical function
- C. Complete relief of pain
- D. Better quality of life
- E. Improved function in family and social roles
- F. Empowerment of the patient

Empowerment of the patient is the overarching goal of therapy for chronic pain. The patient is the primary expert on the pain and its response to treatment, as well as what constitutes realistic goals for therapy. Patient self-report is the most reliable indication of the presence and intensity of pain (C level recommendation), and similarly, the patient provides critical input about the level of pain reduction needed for improved quality of life. Complete relief of chronic pain is seldom a realistic goal, although reduction in its severity is obviously an important goal. This should be made clear in the initial partnership with the patient to address chronic pain.

Improving physical function is another major goal of treatment; explicit steps toward this end should be negotiated with the patient (C level recommendation). However, improved physical function will not translate to a full return to work for many chronic pain patients. Requiring it as a mark of success (or to continue to "deserve" opioids) would be a mistake.

Depression is a common response to chronic pain, and preexisting depression may be a risk factor for its development (C level recommendation). All patients with chronic pain should be assessed for this, along with other psychological comorbidities. Family issues also commonly arise and should be addressed. Improved function in family and other social roles is an important goal to include in the treatment plan for chronic pain (C level recommendation). Input from other family members (particularly the spouse) may be quite helpful in assessing the response to treatment of chronic pain.

---

4. A 72-year-old male is brought to your office by his daughter for a routine follow-up visit. He is blind and has type 2 diabetes. He is taken care of at home by the daughter. He states that he is doing "okay" and that his peripheral neuropathy and activity level have remained the same since his last visit 3 months ago. His daughter seems frustrated and reports that his pain is worse, and that his level of activity has decreased. When asked to give an example, she says, "Trust me, his pain is worse." Your examination reveals nothing remarkable, and the patient's HbA1c level is 6.3%.

You decide to

- A. have the patient and daughter start a patient pain and activity log
- B. prescribe an anxiolytic for the daughter to relieve her stress

C. increase the patient's neuropathic pain medication

The issues of communication, social relationships, psychological well-being, caregiving needs, and spirituality combine to define a complex set of roles, experiences, and perspectives in the care of loved ones. Frequently, caregivers report higher levels of pain and immobility than the patient. On the other hand, patients may be hesitant to admit that they need more care (Evidence level II). They may understate their pain due to an increased concern for caregiving needs and future dependency.

Scheduling time with the daughter would help her better understand the signs of pain, and the factors that influence how patients report their pain (Evidence level III). A way to obtain a more accurate representation of the patient's health would be to create a daily patient pain and activity log. Meeting with the daughter would also facilitate a review of the health system to ensure that she has the community and psychological support services that she needs (Evidence level III). This can help prevent anxiety and depression and reduce unnecessary prescribing of medications. While there are conflicting reports of pain and activity levels, the evaluation reveals good control of the patient's glucose levels. In this case, increasing pain medication would not be indicated. Neither of these two decisions addresses the patient-caregiver relationship.

---

5. True statements regarding chronic pain include which of the following? (Mark all that are true.)

- A. It persists after the initial injury has healed
- B. It can be associated with hyperalgesia
- C. It can be associated with allodynia
- D. It can spread to non-injured areas
- E. It is associated with structural changes in the central nervous system

Patients and their physicians are familiar with acute pain or pain caused by injury. Injury leads to inflammation and changes within the central nervous system. Pain signals are sent to the brain. The brain in turn signals the muscles, causing a reflex muscle spasm. These changes protect the injured area. The tightening of the muscles forms a natural cast around the injury, and the negative sensation of pain promotes learning how to avoid similar injury in the future. As tissues heal, inflammation resolves and the central nervous system sends out fewer signals, resulting in decreased pain and decreased muscle spasm.

Less is known about the etiology of chronic pain. Chronic pain often occurs in the absence of ongoing illness or after healing is complete, and often begins with an injury that causes inflammation and central nervous system changes. The injured area heals, scar tissue is produced, and the inflammation resolves. But, for an unknown reason, the nervous system continues to send pain signals to somatic muscles, as though a new injury were occurring. The nervous system reacts to the memory of the original injury and sends signals similar to those sent in response to that injury. These signals become a disabling message, reminding the patient of the injury (C level recommendation). Hyperalgesia results when second-order neurons at the level of the dorsal horn become more sensitive to peripheral stimuli. They demonstrate increased numbers of action potentials and spontaneous discharges in response to painful stimuli. This increased number of action potentials is experienced as an elevated response to painful stimuli that were previously perceived as less painful (C level recommendation).

Allodynia is the perception of pain caused by usually nonpainful stimuli, such as touch or vibration. Allodynia results from a redistribution of central terminals. Mechanoreceptors establish new synapses with dorsal horn cells that normally receive nociceptive input. After redistribution, mechanoreceptors stimulated by touch or vibration will activate pain pathways in the same way they are activated by nociceptive neurons in response to pain (C level recommendation).

The spread of pain occurs because of an increase in the size of receptive fields within the dorsal horn. Pain perception

then spreads to involve areas that are not normally innervated by the injured nerve.

Nerve injury may result in multiple changes within the central nervous system that perpetuate the pain experience. Increased numbers of action potentials cause hypersensitivity to pain. Redistribution of synapses for mechanoreceptors causes allodynia. Increased receptive field size results in the spread of pain. The use of exercise and psychologic treatment may be effective in chronic pain because these treatments retrain the nervous system to reestablish more normal neural connections (C level recommendation).

---

## Legal\Psychosocial

6. You are seeing a colleague's patient for a follow-up visit. The patient has been taking opioids for 12 months for chronic low back pain. After reviewing his chart you notice numerous phone messages from the patient asking for early refills, as he has been using his opioids more frequently than prescribed. During the encounter, the patient admits to borrowing pain medications from his wife.

In the absence of other aberrant behavior, this is highly indicative of:

- |                     |
|---------------------|
| A. Dependence       |
| B. Addiction        |
| C. Pseudoaddiction  |
| D. Drug trafficking |

The suspicion of opioid addiction in chronic pain sufferers is often triggered by the occurrence of what have been called aberrant drug-related behaviors. Ambiguities inherent in this approach affect patient care adversely. Rather than consistently signifying abuse or addiction, these behaviors are often motivated by undertreated pain.

The term pseudoaddiction was coined in 1989 to describe chronic pain victims mistakenly diagnosed as suffering from opioid addiction when undertreated pain led to certain drug-related behaviors. Simply stated, pseudoaddiction is a misdiagnosis that results from undertreatment of chronic pain. Patients are frequently harmed by the misdiagnosis of addiction and these behaviors should prompt an aggressive search for undertreatment of pain. Unfortunately, this usually does not happen. Instead, when a patient displays certain behaviors, he or she is typically threatened with termination of treatment, rather than questioned about its effectiveness.

Undertreatment of chronic pain should be considered first on the list of differential diagnoses when considering the cause of worrisome drug-related behaviors. Some of these behaviors include

- borrowing another patient's drugs
- obtaining prescription drugs from nonmedical sources
- unsanctioned dosage escalations
- aggressive complaining about the need for higher doses
- drug hoarding during periods of reduced symptoms
- requesting specific drugs
- acquisition of similar drugs from medical resources

(Evidence level III)

The diagnosis of opioid addiction should be based on observation of deteriorating function, which can be directly attributed to opioid abuse, rather than inferred from an anecdotal set of behavioral criteria derived from medical folklore. Behaviors suggestive of opioid addiction include injection of substances prescribed for oral use, concurrent use of related illegal drugs, and selling prescription drugs (Evidence level III).

When patients are obtaining opioids from more than one medical source, the primary physician must reevaluate the pain syndrome. Factors to consider include whether the patient is undermedicated, whether the syndrome is misdiagnosed, and whether the patient is abusing or diverting drugs.

Physicians must work with chronic pain patients to adequately evaluate and treat their pain. In turn, physicians must expect patients to use only one source to obtain opioid prescriptions. A written opioid use agreement is recommended.

---

7. True statements regarding physical dependence on opioids include which of the following? (Mark all that are true.)

- A. Physical dependence develops in most patients taking opioids on a regular basis for more than a few weeks
- B. Physical dependence is a marker of addiction
- C. Withdrawal symptoms develop after abrupt cessation of the opioid
- D. Physical dependence explains why patients take higher doses than prescribed
- E. Physical dependence explains the symptoms produced by administration of an opioid antagonist, such as naloxone (Narcan)

The American Pain Society, the American Academy for Pain Management, and the American Society of Addiction Medicine have jointly created definitions for both physical dependence and addiction. Physical dependence is defined as "a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist." It is an expected consequence of chronic opioid use and is distinct from addiction, which is defined as "a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving" (C level recommendation).

Withdrawal symptoms may be provoked by sudden cessation of the opioid, rapid dose reduction, malabsorption or metabolic changes leading to reduced levels, and/or administration of an antagonist. Physical dependence does not explain why a patient would take a higher dose than what was prescribed (Evidence level III).

---

8. Which one of the following is true regarding the use of agreements or contracts for patients using opioids for chronic pain?

- A. Written agreements reduce the rate of addiction and abuse
- B. Contracts provide the physician with legal protection
- C. Contracts are often recommended by experts in chronic pain management
- D. Contracts have been shown to improve the patient-physician relationship

Contracts or formal agreements are frequently recommended by experts in chronic pain management, discussed extensively in related literature, and used by many physicians. While certain goals of contracts could be supported by virtually all (clarifying plans for use, providing informed consent, and reducing the risk of addiction), consideration of their use should include an understanding of their potential negative consequences. They may damage the patient-physician relationship, erode the patient's sense of trust and reliance on the physician's beneficence, or provide a false sense of security for both the patient and the physician about the risk of addiction (C level recommendation). Finally, no studies have demonstrated a reduction in the incidence of addiction or abuse when contracts are used

(Evidence level III).

Physicians should be familiar with the legal requirement of their own states, but the Federation of State Medical Boards model policy on the use of controlled substances for pain states that the physician should consider a written agreement for patients at high risk for medication abuse, or for those with a history of substance abuse (C level recommendation).

---

9. The Federation of State Medical Boards has published guidelines for the treatment of pain with controlled substances. These guidelines recommend which of the following? (Mark all that are true.)

- A. Documentation of a complete history and physical examination
- B. Documentation of the patient's treatment plan, including ways to measure treatment response
- C. An accurate record of the medications prescribed and a follow-up plan
- D. Having the patient return at appropriate intervals for reevaluation
- E. A contract or written agreement between the patient and the physician

A contract or written agreement is not required by the Federation of State Medical Boards (FSMB) but should be considered if the patient is at high risk for medication abuse. A contract typically includes medication dosages, the frequency of visits, and information about refills of prescriptions. The guidelines do require a documented treatment plan and ways to measure treatment response should be included. Also required are an accurate record of the medications and a follow-up plan. Central to a good record, and an FSMB requirement, is documentation of a complete history and physical examination. The FSMB and other pain experts believe that the patient should be seen at appropriate intervals to reevaluate the treatment plan and assess the patient (C level recommendation for all recommendations).

---

### **Cancer/Terminal Illness**

10. A 40-year-old male has had low back pain for 2 years. He asks your advice concerning physical therapy. Which of the following would be appropriate advice? (Mark all that are true.)

- A. Prescribed exercise programs are the most efficacious physical modality for chronic back pain
- B. Transcutaneous Electrical Nerve Stimulation (TENS) units produce modest benefits in pain reduction
- C. Regular massage therapy produces benefits lasting months to years
- D. While expensive, multidisciplinary rehabilitation programs (including conditioning and cognitive-behavioral components) are clearly beneficial
- E. Hydrotherapy is ineffective for chronic back pain

It is difficult to analyze the evidence for the efficacy of physical therapy, because improvement is affected by a patient's effort and motivation, as well as the personal attention one gets from the physical therapist. Randomized, controlled trials are difficult to perform and compare. On this subject, systematic reviews and meta-analyses do not always agree.

A review of physical modalities for chronic back pain published in 2004 looked not only at efficacy, but also at the clinical significance of the effect. Only exercise programs and multidisciplinary rehabilitation programs (which can cost thousands of dollars) were shown to be effective and clinically beneficial. Laser therapy, spinal manipulation, and massage were shown to be mildly effective with little lasting clinical benefit. Using the same criteria, TENS, magnets, ultrasound, hydrotherapy, and traction were ineffective. There was too little evidence to rank acupuncture, back schools, and lumbar supports.

Physical therapists not only administer modalities but also provide functional assessments, patient evaluations, and

patient education. Therapists can specialize in areas such as neurologic rehabilitation, wound management, or sports training.

---

11. Mind-body therapy (MBT), such as relaxation, (cognitive) behavioral therapies, meditation, imagery, biofeedback, and hypnosis, is used for several common clinical conditions. There is good evidence to support which of the following statements about MBT? (Mark all that are true.)

- A. MBT is more effective for decreasing pain intensity than for improving functional status associated with low back pain
- B. MBT has NO significant effect in the symptomatic treatment of arthritis
- C. Stress management training can be as effective as tricyclic antidepressants in the management of chronic tension-type headache
- D. The combination of relaxation training and thermal biofeedback is the preferred behavioral treatment for recurrent migraine disorder

Multimodal mind-body therapy (MBT) treatments typically include some combination of relaxation, biofeedback therapy, cognitive strategies (e.g., for coping with pain), and education. Narrative reviews suggest that the Arthritis Self-Management Program (ASMP) might be a particularly effective adjunct in the management of arthritis (Evidence level III). This community-based program consists of education, cognitive restructuring, relaxation, and physical activity to reduce pain and distress and facilitate problem solving. Using this program, reductions in pain were maintained 4 years after the intervention, and physician visits were reduced by 40% (Evidence level II).

A review of the efficacy of MBTs in chronic low back pain concluded that there was strong evidence (defined as generally consistent findings in multiple high-quality randomized, controlled trials) that MBTs, when compared with wait-list controls or usual medical care, have a moderate positive effect on pain intensity and only small effects on functional status and behavioral outcomes (Evidence level I, Cochrane review).

A review of the efficacy of relaxation and biofeedback in recurrent migraine headache showed a 43% reduction in headache activity in the average patient compared with a 14% reduction with placebo medication and no reduction in unmedicated subjects (Evidence level II). A more recent narrative review concluded that a combination of relaxation training and thermal biofeedback is the preferred behavioral treatment for recurrent migraine disorder (C level recommendation). Recent evidence indicates that stress management training is as effective as tricyclic antidepressants in the management of chronic tension-type headache, suggesting that combining these two therapeutic approaches might be more effective than using either one alone (Evidence level I).

---

12. A 40-year-old female with three children has chronic low back pain and frequent tension headaches. In addition, she was recently treated for shoulder pain. Her neighbor has suggested that she look into acupuncture and she asks you if acupuncture is safe and effective.

Which of the following would be accurate advice? (Mark all that are true.)

- A. In a randomized study of chronic headache, those treated with acupuncture in addition to usual therapy had fewer headaches than controls
- B. The addition of acupuncture to diclofenac (Voltaren) in patients with shoulder pain improves function more than diclofenac alone

C. Studies that looked at more than 60,000 acupuncture treatments showed no serious adverse events

Acupuncture has been practiced for thousands of years and has been used for hundreds of different ailments. Studies of the method use sham treatments or minimal treatments as controls. Studies often show conflicting results or small clinical effects. Acupuncture is quite safe, with no serious adverse effects reported in two studies including more than 60,000 treatments. Infection is minimized by using disposable needles and aseptic technique. Serious bleeding is very rare.

In a meta-analysis of chronic back pain studies, acupuncture proved to be more effective than sham acupuncture or no treatment. For short-term pain relief in these patients it does not appear to be superior to other active therapies. It was not particularly effective in acute back pain (Evidence level I).

As an adjunct to usual therapies, acupuncture has proven effective in randomized studies of chronic headache and osteoarthritis of the knee (Evidence level I). It is used as an adjunct in cancer pain management. One randomized, controlled trial of auricular acupuncture showed a positive effect in decreasing cancer pain when used with routine analgesics.

---

13. Which one of the following is true regarding the use of glucosamine and chondroitin sulfate in the management of chronic osteoarthritis pain?

- A. Treatment with chondroitin sulfate is associated with a significant decrease in the incidence of joint swelling, effusion, or both
- B. Glucosamine and chondroitin sulfate in combination works as fast as celecoxib (Celebrex)
- C. Glucosamine increases the risk of ischemic cardiovascular events for patients with diabetes mellitus
- D. The use of glucosamine and chondroitin sulfate is more beneficial for mild osteoarthritis pain than for moderate to severe pain

The dietary supplements glucosamine and chondroitin sulfate have been advocated, especially in the lay media, as safe and effective options for the management of symptoms of osteoarthritis. Glucosamine and chondroitin sulfate are the most widely used dietary supplements for osteoarthritis, with estimated sales in 2004 approaching \$730 million. Several studies have evaluated the efficacy of glucosamine and chondroitin sulfate. Some of these studies have shown that these supplements are effective, but have been criticized as having flaws such as failure to adhere to the intention-to-treat principle, enrollment of small numbers of patients, potential bias related to sponsorship of the study by the manufacturers of the dietary supplements, and inadequate masking of the study agent.

The Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) was a randomized, double-blind, controlled, multicenter trial sponsored by the National Institutes of Health. It was designed to rigorously evaluate the efficacy and safety of glucosamine and chondroitin sulfate, separately and in combination, in the treatment of pain due to osteoarthritis of the knee. Both placebo and celecoxib were used as control agents.

The GAIT trial showed that glucosamine and chondroitin sulfate, alone or in combination, did not reduce pain effectively in the overall group of patients with osteoarthritis of the knee. Exploratory analyses suggested that the combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate to severe knee pain (Evidence level I).

Treatment with chondroitin sulfate was associated with a significant decrease in the incidence of joint swelling, effusion, or both. There was no increased risk of ischemic cardiovascular events among patients who also received celecoxib, or among patients with diabetes who received glucosamine.

In the United States, glucosamine and chondroitin sulfate are regulated as dietary supplements and are not held to the more stringent standards for pharmaceuticals. Substantial variation exists between the content listed on the labels of these products and the actual product. Because the GAIT trial was conducted under pharmaceutical rather than

dietary supplement regulations, agents identical to the ones used in the study may not be commercially available (Evidence level III).

In making therapeutic decisions, physicians and patients alike should be aware of data suggesting that celecoxib has a much faster time to response than glucosamine, chondroitin sulfate, or the two in combination. Continuing research is needed to establish the potential efficacy and increase our understanding of the biology, pharmacology, and pharmacokinetics of these agents.

---

14. A 40-year-old male has chronic pain after three back operations. In discussing his overall health you discover that he gave up walking a year ago because of pain, and he has gained 10 lb in the last year. He asks you if relaxation therapy would help his pain.

You consider the use of exercise, relaxation, or behavioral treatments to manage the patient's chronic back pain. True statements regarding this situation include which of the following? (Mark all that are true.)

- A. A Cochrane review found that interdisciplinary biopsychosocial rehabilitation for >100 hr decreased pain and improved function
  - B. Multiple meta-analyses have shown that cognitive therapy modestly reduces chronic back pain
  - C. Passive modalities for back pain, such as TENS, relaxation, and massage, are recommended in place of active exercise regimens for patients with limited mobility
  - D. Learning to use the relaxation response has been shown to reduce clinic visits by chronic back pain patients
- 

Multiple studies and several guidelines agree that exercise and fitness are a key component in relieving chronic back pain. No particular type of exercise demonstrates a clear advantage over any other. Guidelines recommend fostering self-management skills in patients and setting goals for functional improvement (Evidence level C). Only very intense interdisciplinary biopsychosocial interventions made a difference when reviewed by the Cochrane group (Evidence level I, Cochrane review). A recent clinical inquiry confirmed the modest effect of cognitive therapies for improving some chronic pain states, and emphasized the efficacy of tricyclic antidepressants in reducing chronic back pain (A level recommendation).

Meditative therapies such as Benson's relaxation response (repetition of a word, phrase, prayer, or other activity to counteract stress) have been studied in a variety of contexts. The studies vary in strength of response, numbers, and quality of controls. It is difficult to make any strong recommendations for chronic pain, but such therapies are relatively low cost and harmless (Evidence level III).

---

15. A patient at 32 weeks gestation asks about her options for the management of labor pain.

Appropriate advice would include which of the following? (Mark all that are true.)

- A. Epidural anesthesia is associated with increased rates of cesarean delivery
- B. Epidural anesthesia is associated with increased instrumentation rates at delivery
- C. Continuous labor support decreases maternal pain during labor
- D. Warm water baths can decrease labor pain for short periods of time

Two large meta-analyses have shown little effect of epidural anesthesia on cesarean delivery rates. Epidural anesthesia provides better pain relief in labor than opioids, but is associated with increased instrumentation rates,

maternal fever, and a slightly longer duration of labor (Evidence level I). A randomized, controlled trial of intrathecal fentanyl showed superior pain relief and shorter labor duration with no increase in cesarean delivery rates compared to systemic hydromorphone (Evidence level I). Reviews of continuous labor support with doulas show decreased rates of operative delivery and decreased requests for pain medication (Evidence level I). Warm water baths appear to decrease pain but have a short duration of action (Evidence level I). Sterile saline injections provide short-term relief of back pain but do not decrease requests for pain medication (Evidence level I). Despite years of use there remains little clear evidence on the safety and efficacy of opioids in labor (Evidence level I).

16. Your patient asks your opinion about seeing the chiropractor one of his friends recommended. Which one of the following would you tell him about the benefits of manipulation for this problem?

- A. Spinal manipulation is more likely to shorten the duration of his pain than any other treatments you may prescribe
- B. Spinal manipulation is more likely to reduce the severity of his pain than any other treatments you may prescribe
- C. Spinal manipulation combined with acupuncture has been found to be the most effective treatment for his type of pain

D. Spinal manipulation does not offer any lasting advantages over the other treatments you usually prescribe

Acute low back pain is an extremely common problem with high costs of care. Spinal manipulation therapy is often recommended, despite contradictory evidence regarding its effectiveness.

A 2004 Cochrane review concluded that spinal manipulation was more effective than sham (placebo) therapy for reducing the severity and duration of pain, and for improving functional ability. However, it has not been shown to be more effective than pain medication, physical therapy, exercise, back school, or usual primary care (Evidence level I, Cochrane review).

---

17. For which of the following conditions do epidural corticosteroid injections have moderate to strong evidence for short term efficacy (i.e., improvement in pain scores and/or quality of life, lasting for weeks)? (Mark all that are true.)

- A. Cervical radiculopathy
- B. Lumbar radiculopathy
- C. Neck pain
- D. Low back pain
- E. Spinal stenosis

Epidural corticosteroid injections can be administered using interlaminar, transforaminal, and caudal approaches. While they are commonly performed by pain specialists, the evidence of efficacy for these procedures is lacking. Multiple systematic reviews have provided conflicting opinions. There is moderate evidence for short-term and long-term relief using interlaminar epidural injections for cervical radiculopathy (evidence level 2). The evidence for epidural injections in managing lumbar radiculopathy was strong for short-term relief and limited for long-term relief (evidence level 2). The evidence is inconclusive in the management of neck pain, low back pain, and lumbar spinal stenosis (Evidence level C). The evidence is strong for short-term improvement and moderate for long-term improvement in the management of nerve root pain.

---

18. Which one of the following is true regarding management of osteoarthritis of the knee?

- A. When prescribing an exercise program, range-of-motion exercises should be included
- B. Tri-compartmental knee arthritis requires surgical treatment
- C. Good results have been reported for total knee arthroplasty in patients over 60 years of age
- D. Arthroscopic lavage should be considered even for patients without mechanical symptoms

Nonpharmacologic osteoarthritis treatment modalities are directed toward weight reduction, joint protection, and energy conservation. The exercise program should include range-of-motion (B level recommendation), aerobic, and muscle strengthening exercises. Patients may also require physical therapy, occupational therapy, assistive devices for ambulation and activities of daily living, and advice regarding appropriate footwear and orthotics (e.g., wedged insoles).

For pharmacologic therapy, the initial drug of choice is acetaminophen, 4 g/day. For patients taking NSAIDs, gastrointestinal (GI) risk should be assessed, including any history of ulcer disease and/or GI bleeding. Other risk factors include the use of high-dose, chronic, or multiple NSAIDs, including aspirin; concomitant use of corticosteroids and/or warfarin (A level recommendation); and age >60 years. A gastroprotective agent should be prescribed for patients determined to be at high risk.

Arthroscopic debridement may be indicated for the treatment of patients with degenerative arthritis with mechanical symptoms, such as locking, catching, or giving way of the joint (B level recommendation). Neither arthroscopic lavage nor debridement is indicated for patients without mechanical symptoms (A level recommendation). Results of arthroscopic debridement in patients with mechanical symptoms are variable, but high success rates are reported if there is no gross malalignment or instability, some articular cartilage remains, and symptoms are well localized (B level recommendation).

Patients with bi- or tricompartmental arthritis of the knee should be considered for total knee arthroplasty only if conservative treatment is unsuccessful (A level recommendation). Good results have been reported in total knee arthroplasty only in patients under 55 years of age (A level recommendation).

---

19. Cultural aspects of pain include which of the following? (Mark all that are true.)

- A. The dominant culture of pain in the United States honors the stoical person
- B. The meaning and expression of pain is influenced by the patient's culture
- C. Persons from cultures different from that of their treating physician often receive inadequate pain management
- D. Pain behaviors can be predicted reliably by understanding a patient's culture
- E. To minimize bias, physicians must be aware of their own pain experiences and culture

Culture is the framework that directs human behavior in a given situation. The meaning and expression of pain are influenced by people's cultural background. Pain is not just a physiologic response to tissue damage, but also includes emotional and behavioral responses based on individuals' past experiences and perceptions of pain. However, not everyone in every culture conforms to a set of expected behaviors or beliefs, so trying to categorize a person into a particular cultural stereotype will lead to inaccuracies. On the other hand, knowledge of a patient's culture may help to better understand their behavior.

Studies have shown that patients from ethnic minorities and cultures different from the health care professionals treating them receive inadequate pain management (Evidence level II). Each of us has the impression that people from distinct cultures are more or less likely to express their pain experience in a manner that is somewhere between

quietly enduring (stoical) or very expressive. While the physician should attempt to treat the expressive patient and the stoical patient alike, physicians from a stoical culture are likely to be more attentive to the patient who is stoical. The culture of pain in mainstream American culture tends to teach the hurting person to be stoical and the attending person to honor that stoicism.

For the physician, even more important than understanding the culture of others is understanding how his or her own upbringing affects attitudes about pain (C level recommendation). It is important to overcome the belief that one's own reaction to pain is "normal" and that other reactions are "abnormal." Even subtle cultural and individual differences between patient and physician, particularly in nonverbal, spoken, and written language, can affect care.

## **Chronic Pain**

20. True statements regarding dysmenorrhea include which of the following? (Mark all that are true.)

- A. Leiomyomata can cause secondary dysmenorrhea
- B. Oral contraceptives will not help primary dysmenorrhea
- C. NSAIDs can be used on an intermittent basis to help with dysmenorrhea
- D. Prostaglandins play a principal role in dysmenorrhea

Dysmenorrhea is pain that occurs during the menses and is crampy in nature. It is commonly classified as either primary or secondary. Primary dysmenorrhea is a condition unto itself that is not a symptom of another disorder. Secondary dysmenorrhea can be caused by leiomyomata or by other pelvic pathology. Prostaglandin release is the understood pathophysiology for primary dysmenorrhea. Oral contraceptives provide relief for primary dysmenorrhea by suppressing ovulation and thereby reducing the release of prostaglandins (Evidence level II). NSAIDs that inhibit prostaglandin synthetase provide relief in most patients and are usually initiated for 2-5 days, just before and during the menses (Evidence level I). In some recalcitrant cases the NSAIDs could be used continuously, with proper attention to the risks of chronic NSAID use.

---

21. A 30-year-old brick mason presents to your office with midback pain. On examination you note that his rhomboid muscles are in spasm, and he jumps when you touch three discrete points in the muscles. He is concerned that he may be developing fibromyalgia like his mother. True statements regarding the differentiation between myofascial pain syndrome and fibromyalgia include which of the following? (Mark all that are true.)

- A. The tender points of fibromyalgia are different from the trigger points seen with myofascial pain syndrome
- B. Muscle spasm is most often associated with fibromyalgia
- C. A jump/twitch response is most often associated with myofascial pain syndrome
- D. The tender points in fibromyalgia patients tend to be distributed asymmetrically
- E. Myofascial pain tends to be regional

The trigger points seen with myofascial pain syndrome are different from the tender points seen with fibromyalgia. Trigger points are discrete, focal, hyperirritable spots located in a taut band of skeletal muscle. Compression of these points is painful and can produce referred pain, referred tenderness, motor dysfunction, and autonomic phenomena. Trigger points may be single or multiple, and are usually asymmetric. Pressing them may elicit a twitch in the muscle or a jump response from the patient. Trigger points are associated with regional pain syndromes. Patients with fibromyalgia exhibit multiple tender points symmetrically distributed along the axial skeleton, and have constitutional

symptoms such as fatigue, sleep disturbance, and depressed mood.

No single modality stands out as the best for long-term treatment of trigger points and myofascial pain. However, trigger point injections are widely accepted and recommended for providing short-term relief (C level recommendation).

Dry-needle techniques usually result in more soreness the next day than injection of local anesthetic. The addition of corticosteroids and other medications to local anesthetics is unnecessary for efficacy and may cause muscle damage. The technique for trigger point injection is well described in the reference article.

---

22. A 52-year-old female with type 2 diabetes sees you for a routine follow-up. Her diabetes is controlled with diet, exercise, and oral antihyperglycemics. While her diabetes has not always been under good control, her last hemoglobin A1c was 6.3%. Her cholesterol is under good control and a recent stress test was negative. At today's visit, she describes a painful numbness in her toes bilaterally. She has been able to continue working but the pain is beginning to interfere with her sleep. After performing a physical examination, you decide to treat her symptoms.

True statements regarding this situation include which of the following? (Mark all that are true.)

- A. A low dose of a tricyclic antidepressant is the preferred initial therapy
- B. SSRIs would be an appropriate first-line therapy if depression were also present
- C. The efficacy of gabapentin is similar to that of amitriptyline
- D. Opioids, alone or in combination with antidepressants, would be effective

Meta-analyses consistently show that tricyclic antidepressants (TCAs) are effective for neuropathic pain (Evidence level I, Cochrane review). They can be of particular benefit where insomnia, anxiety, or depression is present. SSRIs are not considered first-line therapy for diabetic neuropathy because the evidence of their effectiveness is limited (Evidence level I). Duloxetine and venlafaxine have demonstrated efficacy in treating neuropathic pain (Evidence level II). An estimated 2.6 patients must be treated with TCAs and 6.7 patients with SSRIs to have one patient with more than 50% pain relief. Gabapentin has a demonstrated efficacy in treating neuropathic pain (Evidence level I, Cochrane review). It is an alternative to TCAs where side effects or contraindications prevent their use. A small randomized, controlled trial showed that gabapentin had an efficacy and tolerability similar to that of amitriptyline (Evidence level II). The efficacy of opioids in the treatment of neuropathic pain has been consistently demonstrated in randomized, controlled trials, but they typically require greater caution than other options (Evidence level I).

---

23. True statements regarding the management of chronic daily headaches include which of the following? (Mark all that are true.)

- A. A small daily dose of prednisone (5-10 mg) helps decrease the frequency of headaches
- B. Amitriptyline can reduce headache frequency by up to 50%
- C. Opioids are effective (50% improvement) in over 60% of patients
- D. NSAIDs are associated with a lower risk of medication overuse headaches compared to ergotamine

Chronic daily headache refers to the presence of a headache more than 15 days per month for longer than 3 months. Chronic daily headache is not a diagnosis but a category that contains many disorders representing primary and

secondary headaches. Secondary causes must be ruled out before the diagnosis of a primary headache disorder is made. Approximately 3% -5% of the population worldwide and 70%-80% of patients presenting to headache clinics in the United States have daily or near-daily headaches. The disability associated with this disorder is substantial and includes a diminished quality of life related to physical and mental health, as well as impaired physical, social, and occupational functioning.

The overuse of medications used for acute headache may lead to medication overuse headache, a syndrome of daily headaches caused by the very medications used to relieve the pain. The prevalence in the population of chronic daily headache associated with overuse of these medications was recently estimated to be 1.4% overall, with a higher estimated occurrence among women (2.6%), especially those over the age of 50 years (5%) (Evidence level II).

Overuse of medications for acute headache is defined as any of the following:

- regular overuse of a headache medication for >3 months
- use of ergotamine, triptans, opioids, and combination analgesics >10 days/month
- use of simple analgesics 15 or more days/month
- use of any headache medications 15 or more days/month

NSAIDs and dihydroergotamine mesylate (unlike ergotamine tartrate) are generally associated with a low risk of medication overuse headache, and are often used to treat breakthrough headaches during the withdrawal period. Randomized trials of the use of preventive medications in chronic daily headache are scarce. In a single trial involving amitriptyline, the frequency of headache was reduced by more than 50% in over half of the study participants (Evidence level I).

A recent double-blind, placebo-controlled study evaluated the effect of 100 mg of prednisone for 5 days on the duration of severe withdrawal headache in 20 patients with presumed medication overuse headache. There was a significant reduction in the number of hours of severe withdrawal headache in the active-treatment group, which confirmed earlier observations from uncontrolled studies (Evidence level I).

The use of daily opioid therapy in patients with chronic daily headache is controversial. A recent prospective study with an initial cohort of 160 patients who were prescribed daily opioid therapy reported the outcomes among 70 patients with medically refractory chronic daily headache who continued this therapy for at least 3 years. Only 41 of the original 160 patients (26%) had an improvement of 50% or more on a headache index that took into account the frequency and severity of headaches each week (Evidence level II). Half of the patients had "problem drug behavior" (defined as "lost" prescriptions, seeking medication from other sources, and most commonly, dosage violations). Most of these patients (74%) either did not show marked improvement or were dropped from the program because of problem drug behavior. These data underscore the low efficacy of long-term opioid therapy and the high risk of misuse in this patient population.

---

24. True statements regarding the management of fibromyalgia include which of the following? (Mark all that are true.)

- A. Tricyclic antidepressants or cyclobenzaprine (Flexeril) at bedtime is an appropriate initial therapy
- B. NSAIDs may be used effectively either as monotherapy or in combination with other medications
- C. Aerobic exercise two to three times per week may improve conditioning and fibromyalgia symptoms
- D. Sleep and anti-anxiety agents such as trazodone (Desyrel), benzodiazepines, and nonbenzodiazepine sedatives are indicated if sleep disturbance is a prominent symptom
- E. Multidisciplinary approaches that incorporate two or more strategies help decrease pain and improve function

The following recommendations regarding the management of fibromyalgia are supported by the strongest evidence (Strength of evidence A: There is evidence of type I, or consistent findings from multiple studies of types II, III, IV). Evaluation of the patient with fibromyalgia syndrome (FMS) begins with a complete history and physical examination, focusing on illnesses that may mimic or complicate FMS, such as hypothyroidism or ankylosing spondylitis, or that can

occur concurrently with FMS, such as tendinitis, systemic lupus erythematosus, rheumatoid arthritis, or osteoarthritis. The clinician should perform a complete joint examination, manual muscle strength testing, and a neurologic examination.

The clinical diagnosis of FMS depends on the presence of widespread pain, defined as pain in all four body quadrants and axial pain, for at least 3 consecutive months. The only physical examination criterion for the diagnosis of FMS is the presence of excess tenderness to manual palpation of at least 11 of 18 muscle-tendon sites.

Multiple strategies, including both pharmacologic and nonpharmacologic therapies, should be used in the management of FMS. For initial treatment of FMS, a tricyclic antidepressant, in particular 10-30 mg amitriptyline, or cyclobenzaprine can be given at bedtime to promote sleep. An SSRI such as fluoxetine, alone or in combination with a tricyclic, can be used for pain relief. NSAIDs should not be used as the primary pain medication. There is no evidence that NSAIDs are effective when used alone, although NSAIDs (including COX-2 selective agents) and acetaminophen may provide some analgesia when used with other medications.

Other potentially useful medications include sleep and antianxiety medications such as trazodone, benzodiazepines, nonbenzodiazepine sedatives, or L-dopa and carbidopa, especially if sleep disturbances such as restless legs syndrome are prominent.

Patients with FMS should be encouraged to perform moderately intense aerobic exercise (60%-75% of age-adjusted maximum heart rate) two to three times per week. In individuals who are deconditioned, this rate can be achieved with very low levels of exercise.

Multidisciplinary approaches incorporating two or more strategies decrease pain and improve function in FMS, especially in people who have not responded to simpler approaches.

---

25. A 59-year-old female has persistent pain months after an acute herpes zoster outbreak in a right T-10 distribution. There are no active lesions and only mild erythema remains where the rash appeared. Her pain is localized to the back. It is persistent and severe and interferes with her daily routines.

Which of the following treatment courses would be good choices? (Mark all that are true.)

- A. Opioid analgesia
- B. Tricyclic antidepressants
- C. Corticosteroids
- D. Anticonvulsants
- E. Nerve blocks

Postherpetic neuralgia can be a severe continuing problem. Opioids can have a role in the treatment of acute herpes zoster outbreaks, but in postherpetic neuralgia should be limited to control of extreme pain when initiating a treatment plan. Antidepressant medications, particularly tricyclics, can be very helpful (Evidence level I). In addition to their role in pain control, they may be helpful in treating the depression that can be seen in almost 90% of patients with postherpetic neuralgia. Corticosteroids are not useful in postherpetic neuralgia. Anticonvulsants such as gabapentin are helpful (Evidence level I). Nerve blocks have been successful in achieving pain relief, as have transdermal anesthetics.

---

### **Acute Pain**

26. A 45-year-old male is evaluated for a chronic cough and chest CT shows a suspicious lesion. An open lung biopsy is planned. The patient has chronic low back pain and takes methadone, 10 mg orally 3 times a day. He has been on this stable dose for several years.

You meet with the patient and anesthesia team to plan for postoperative pain management. True statements regarding this situation include which of the following? (Mark all that are true.)

- A. The usual dose of methadone should be continued before and on the day of surgery, and restarted postoperatively
- B. Alternative analgesia (e.g., epidural) should be used in the postoperative period while he is NPO
- C. For moderate to severe pain, patient-controlled analgesia and epidural analgesia have a similar efficacy
- D. The failure rate for epidural analgesia exceeds 15%
- E. Compared to NSAIDs, acetaminophen provides comparable analgesia for postoperative pain

Methadone is a synthetic long-acting opioid used for chronic pain management and treating opioid addiction. All patients on methadone, whether for methadone maintenance treatment or pain management, should continue the dose before and on the day of the surgery to avoid unnecessary fluctuation of the drug level (C level recommendation). The practice of abrupt discontinuation of methadone before surgery is unjustifiable. Patients should resume oral methadone as soon as they can tolerate oral fluids well. During the period of fasting in the postoperative period, patients should receive alternative analgesia such as intravenous patient-controlled analgesia or regional analgesia/anesthesia (C level recommendation).

While patient-controlled analgesia (PCA) and epidural analgesia are commonly used for postoperative pain control, epidural analgesia is generally considered more effective. There is a lower incidence of moderate to severe pain and severe pain when an epidural is used (20.9% and 7.8% respectively) compared with PCA (35.8% and 10.4%) (Evidence level I). Large prospective studies of epidural analgesia report a 17.4% analgesic failure rate (e.g., catheter dislodgement, unilateral block, missed segment).

In major surgery, the efficacy of NSAIDs and acetaminophen seems to be comparable (Evidence level I).

Acetaminophen is a viable alternative to NSAIDs, especially because of the low incidence of adverse effects, and should be the preferred choice in high-risk patients (C level recommendation).

---

### Pharmacologic Management

27. A 40-year-old male with chronic hepatitis C has osteoarthritis in his knees that is beginning to limit his activity. He asks you if he can take acetaminophen for the pain.

Which of the following would be appropriate advice? (Mark all that are true.)

- A. Acetaminophen overdose is a leading cause of fulminant liver failure in adults
- B. Acetaminophen is excreted through the biliary system
- C. He can safely take up to 3 grams of acetaminophen per day
- D. NSAIDs are preferred over acetaminophen in patients with chronic liver disease

Acute acetaminophen overdose is a very common problem in the United States, and when unrecognized can lead to fulminant hepatic failure. In healthy adult nondrinkers, acetaminophen is safe taken chronically in doses up to 4 g/day. Adults who drink excessively, those with chronic liver disease, and those with malnutrition are at increased risk for toxicity. Acetaminophen should be limited to 2 g/day in these persons (B level recommendation). It appears safe at this dosage, and is preferred over NSAIDs in patients with chronic liver disease. Acetaminophen is metabolized in the liver and excreted by the kidneys.

---

28. Common adverse effects of NSAIDs include which of the following? (Mark all that are true.)

- A. Renal toxicity
- B. Gastrointestinal bleeding

- C. Peripheral edema
- D. Increased systolic blood pressure

NSAID use is associated with renal toxicity, gastrointestinal bleeding and ulcers, peripheral edema, and increased systolic blood pressure (median 5 mm Hg) (Evidence level I).

---

29. A 70-year-old male has significant osteoarthritis in his knees. After failing conservative measures, he is evaluated for bilateral knee replacement and expects to undergo surgery in the next few weeks. For pain management, you have prescribed acetaminophen, 1000 mg orally four times daily, but the patient is still having significant pain. You wish to improve his pain control with the use of an acetaminophen/opioid or NSAID/opioid combination.

True statements regarding these medications include which of the following? (Mark all that are true.)

- A. Combination medications may improve pain control while limiting the side effects associated with a higher dose of a single agent
- B. Propoxyphene/acetaminophen (Darvocet N-100) provides pain control similar to that of acetaminophen alone
- C. Codeine may be ineffective in up to 10% of African-American patients, due to a cytochrome P450 enzyme deficiency
- D. When the maximum dosage of the acetaminophen or NSAID component is reached without sufficient pain relief, adding a pure opioid to the nonopioid is recommended
- E. Unsupervised use of over-the-counter medications along with combination medication increases the risk of adverse events

The agents in combination medications operate through different mechanisms. Their use in combination can reduce the side effects of a higher dosage of a single agent. A meta-analysis of 26 trials involving 2,231 patients compared the combination of acetaminophen and propoxyphene (Darvocet) to acetaminophen alone and found that the combination provided little benefit over acetaminophen (Evidence level I). To become active, codeine is metabolized to morphine; it may not be metabolized in up to 10% of Caucasians, due to a cytochrome P450 deficiency. Combination medications are limited by their NSAID or acetaminophen content. When the maximum dosage is reached, switching to non-combination medications is recommended (C level recommendation). Without express warnings, patients may use over-the-counter medications that contain acetaminophen or NSAIDs. Unsupervised use of these medications increases the risk of adverse events.

---

30. True statements regarding the use of the fentanyl transdermal patch (Duragesic) include which of the following? (Mark all that are true.)

- A. According to the FDA, it should not be used for postoperative pain
- B. It should be prescribed at the lowest dose needed when used on an as-needed basis
- C. Patients may have a sudden rise in their body level of fentanyl if they become hypothermic
- D. Because fentanyl is absorbed transdermally, other medications do not affect its plasma levels

The FDA is investigating reports of death and other serious adverse events related to narcotic overdose in patients using the fentanyl transdermal patch for pain control. In June 2005 the Duragesic product label

was updated to add new safety information in several areas of labeling, and a "Dear Healthcare Professional" letter about these changes was issued by the manufacturer.

The directions for use of the fentanyl transdermal patch must be followed exactly to prevent death or other severe side effects from overdosing. These directions are provided in the product label and patient package insert.

The fentanyl transdermal patch is a long-acting medication and should not be used for intermittent pain, short-term pain, or postoperative pain (C level recommendation). Pain after an operation improves with time and requires a shorter-acting pain medication for PRN use and for easier titration downward. The patch delivers a steady level of medication around the clock and cannot be used for breakthrough pain. Patients on the fentanyl patch may have a sudden increase in their fentanyl plasma concentration if they have an increase in their body temperature or are exposed to heat or use other medicines that increase the elimination half-life of fentanyl. Ketoconazole is a cytochrome P450 3A4 inhibitor, which is one type of drug that can have this effect. Compared to other opioids, fentanyl patches are relatively expensive and are less flexible in terms of dosage titration.

---

December 21, 2007 — A public health advisory has been issued to educate healthcare professionals and patients regarding the appropriate use of fentanyl transdermal patches (*Duragesic*, Alza Corp and generics), the US Food and Drug Administration (FDA) advised healthcare professionals today. Despite a previous public health advisory and safety labeling changes issued in July 2005, the FDA has continued to receive reports of death and life-threatening adverse events related to fentanyl overdose.

As before, factors included use of the patches in opioid-naive patients, concomitant use of more patches than prescribed, too-frequent patch replacement, and patch exposure to heat, according to an alert sent from MedWatch, the FDA's safety information and adverse event reporting program. Healthcare professionals are reminded that the fentanyl skin patch is only indicated for management of persistent, moderate to severe chronic pain in opioid-tolerant patients aged 2 years and older who require a total opioid dose at least equivalent to a 25 µg/hour patch. Because of the risk for potentially fatal respiratory depression, the patch is not indicated for the management of postoperative, mild, or intermittent pain. The FDA notes that concomitant use of cytochrome P450 3A4 isoenzyme (CYP 3A4) inhibitors (eg, ketoconazole, erythromycin, nefazodone, diltiazem, and grapefruit juice) can increase fentanyl plasma concentrations and the risk for respiratory depression. If the drug combination cannot be avoided, patients should be carefully monitored; adjustment of the fentanyl dose may be required.

Patients should be advised to use the patch exactly as prescribed and only if they have been regularly taking other strong narcotic pain medications for at least a week. Heating pads, electric blankets, saunas, heated waterbeds, hot baths, and sunbathing can increase fentanyl exposure and should be avoided. If a patch falls off before 72 hours have elapsed, the patch should be safely discarded and another applied. Patients should be instructed to call their healthcare provider if this occurs or if they have trouble breathing or have slow/shallow breathing; slow heartbeat; severe sleepiness; cold, clammy skin; trouble walking or talking; or feel faint, dizzy, or confused.

---

31. True statements regarding the use of methadone for chronic non-cancer pain include which of the following?

(Mark all that are true.)

- A. Because of methadone's long half-life (>20 hours), it should be avoided in elderly patients
- B. Methadone's analgesic effect builds over 5-7 days, producing a duration of analgesia nearly equivalent to its half-life
- C. Methadone is metabolized principally by the liver and should not be used in patients with hepatitis C
- D. Methadone, unlike morphine, does not require adjustment for renal disease
- E. Methadone can be used safely in patients allergic to morphine

Methadone is a synthetic opioid with a half-life of about 22 hours. The duration of analgesia is shorter than the half-life, but typically builds to 8-12 hours with repeated dosing. Methadone accumulates in the tissues, and serum levels build gradually over 5-7 days. Dosing adjustments should not be made more frequently than every 5-7 days in the outpatient setting (C level recommendation).

While methadone is metabolized by the liver, it is usually unnecessary to adjust methadone doses for hepatic disease. A minor portion of methadone is cleared by the kidneys and it is usually unnecessary to adjust dosing for renal failure. Because methadone is synthetic, it can be used in patients with a true allergy to morphine. Methadone should be used with caution in the elderly patient, and a lower initial dose may be appropriate (C level recommendation).

---

32. True statements regarding the use of tramadol (Ultram) include which of the following? (Mark all that are true.)

- A. It is a  $\mu$  opioid-receptor agonist
- B. It may lower the seizure threshold
- C. It is an effective agent for neuropathic pain
- D. It can cause serotonin syndrome when used with SSRIs

Tramadol is a weak  $\mu$  agonist. It also causes both norepinephrine and serotonin reuptake inhibition and has the potential to lower the seizure threshold. In a surveillance study, the risk of seizure was increased two- to sixfold among users, adjusted for selected comorbidities and concomitant drug use (Evidence level III). The risk was highest among those aged 25-54 years, those with more than four tramadol prescriptions, and those with a history of alcohol abuse, stroke, or head injury. There is also a risk of serotonin syndrome when tramadol is used with SSRIs. Tramadol has demonstrated benefits in neuropathic pain (Evidence level I). Tramadol's side effects include nausea, constipation, and dizziness. Its side effect profile is similar to that of codeine.

---

33. A 62-year-old female with metastatic cancer of the colon is expected to die within weeks. She has had pain in her right chest where a large pulmonary metastasis has been identified. This pain has been well controlled with sustained-release morphine, 60 mg twice daily.

What is the most appropriate dose of immediate-release morphine for breakthrough pain every 1-2 hours on an as-needed basis?

- A. 10 mg
- B. 30 mg
- C. 60 mg
- D. 120 mg

Most experts recommend a starting dose for breakthrough pain of 10%-25% of the total daily dose, to be adjusted according to the patient's response. An oral opioid dose may be repeated after 1 hour if the response is inadequate. The patient should be instructed that recurrent need for more than one dose per episode of pain is an indication for dosage adjustment, and the physician should be contacted. Similarly, a regular need for breakthrough medication suggests that the sustained-release dosage should be reassessed.

---

34. A 30-year-old male with AIDS-related neuropathy is experiencing incomplete pain control. He asks you if dronabinol (Marinol) or another cannabinoid is likely to help his pain. Which of the following would be accurate advice?

- A. Oral cannabinoids are not associated with CNS depression or psychotropic effects
- B. Cannabinoids such as dronabinol are no more effective than codeine
- C. Dronabinol has been shown to be effective as an adjunct to opioids in treating neuropathic pain
- D. Smoking cannabis has been shown to decrease self-reported pain scores in men with complex regional pain syndrome

A qualitative systematic review in the *British Medical Journal* examined the safety and efficacy of cannabinoids for treatment of pain. It showed that cannabinoid doses equivalent to 5-20 mg of 9-THC were no more effective than 50-120 mg of codeine, and some were no better than placebo (evidence level I). Codeine is the least effective opioid agent. In this study, cannabinoids were commonly associated with central nervous system depression and undesirable psychotropic effects. Their usefulness for pain control is therefore quite limited.

---

35. True statements regarding tricyclic antidepressants include which of the following? (Mark all that are true.)

- A. Analgesic efficacy and side effects are both dose related
- B. Because of the anticholinergic side effects, tertiary amines such as amitriptyline should be avoided in elderly patients
- C. Amitriptyline has demonstrated benefits for acute pain, neuropathic pain, fibromyalgia, and low back pain
- D. While tricyclic antidepressants can exacerbate existing cardiac conduction abnormalities, this problem does not arise with the doses typically used for pain management
- E. The onset of effect for pain relief is similar to that required for an antidepressant effect

Tricyclic antidepressants (TCAs) have been studied in a number of controlled trials and have demonstrated benefits as analgesics (evidence level I). Amitriptyline has been studied most thoroughly and is efficacious in a number of pain states, including acute pain, neuropathic pain, fibromyalgia, and low back pain. Amitriptyline is a tertiary amine and has significant anticholinergic side effects, including dry mouth, constipation, urinary retention, sedation, and weight gain. For these reasons, amitriptyline should be avoided in the elderly (C recommendation). The secondary amines (desipramine, nortriptyline) have less anticholinergic activity and may be better tolerated.

Cardiac conduction abnormalities, recent cardiac events, and narrow-angle glaucoma are contraindications to using tricyclic antidepressants. Both analgesic efficacy and side effects are dose dependent, with analgesic efficacy occurring at doses lower than those required to treat depression. Remarkably, analgesia from TCAs occurs in the absence of depression or in cases with no antidepressant effect. The onset of analgesia occurs within 1 week, compared to the 3 weeks required for an antidepressant effect.

---

36. True statements regarding opioid-induced respiratory depression include which of the following? (Mark all that are true.)

- A. It generally occurs in opioid-naive patients
- B. Pain reduces this effect

C. It is rare when opioids are appropriately titrated

D. It occurs commonly in patients with COPD

Respiratory depression generally occurs in opioid-naive patients given excessive initial doses (evidence level III). It is rare when opioids are appropriately titrated, even when aggressive rapid titration is required in the face of severe pain. This side effect of opioids is reduced by pain, and sudden relief of pain (such as successful nerve block or a dramatic response to an adjuvant analgesic) may require rapid downward titration of the opioid in order to avert respiratory depression. Patients with underlying respiratory disease, including COPD, may be more vulnerable to respiratory depression, but even in these patients respiratory depression remains rare when appropriate titration is used.

---