

Challenging and Changing the Experience of Pain:

Acute Pain Management in the Perioperative Setting in Patients with a Substance Abuse History

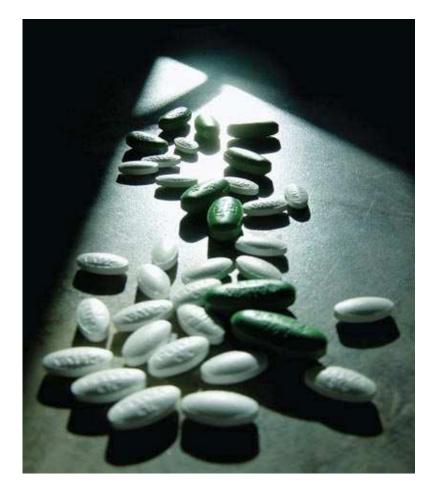
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ostoperative pain management presents a challenge in all sur gical patients, particularly patients with a history of substance abuse. The current perioperative pain management protocol for recovering substance abuse patients, specifically those with a history of opioid addiction, is inadequate. Most patients undergoing a surgical procedure are treated with the same pain management assess ment tools and medications with little regard for current addictions or recovering substance abuse patients.

LEARNING OBJECTIVES

- Identify the differences for administering pain control to patients who suffer from addiction versus those who do not.
- Define the physical and emotional components of pain.
- Describe the etiology of addiction.
- Evaluate the factors used to assess a patient's pain level.
- Assess the benefits of MMT

Prevention of withdrawal or relapse is mostly ignored; however, simple and manageable changes made in hospital policy, patient and staff education and patient assessment can improve this practice. Medication protocol can be individualized. All of these changes in practice can greatly enhance the care needed by this special population of patients by individualizing care rather than treating this population with no regard for their preexisting disease. Whether the patient is an active substance abuser or in recovery and working on a 12-step program, the patient's emotional, physical and psychological reaction to



pain is much different than a patient that has not suffered from addiction. Because of this abnormal reaction, the treatment chosen to control pain should be altered in order to meet the needs of this special population.¹

This issue greatly impacts practice as a surgical team member. The attitude of, "once a drug addict, always a drug addict," needs to be altered. All patients, regardless of history, need equal treatment in regards to pain management in accordance with the Patient's Bill of Rights in the United States.^{2, 3} Just as a patient with a disease process, such as diabetes, has special needs, the substance abuse patient's plan of care for postoperative pain management should be augmented accordingly.⁴

Opioid-addicted patients, in particular, pose a great challenge in the postoperative setting.^{4, 5, 6} Since pain is such a broad topic with multiple facets, the research for this topic is limited to the patient suffering from past or present opioid addiction. The majority of the medications used in practice for postoperative pain management are opioid-based. Fear of triggering a craving in the recovering patient, or not managing the required serum drug levels to prevent withdrawal symptoms in the active patient while managing postoperative pain, is of constant concern. Pain, as defined by Webster's Medical Dictionary, is an unpleasant sensation that can range from mild, localized discomfort to agony. The word is derived from the Latin word poena, meaning a fine or a penalty. Pain has both physical and emotional components. The physical part of pain results from nerve stimulation and may be contained in a localized area, such as in an injury, or it can be more diffuse. The emotional components of pain range from anger and sadness to severe depression.7,8

In today's clinical practice, however, the most widely accepted definition of pain is the definition set forth by Margo McCaffery in 1968, which states that, "pain is whatever the experiencing person says it is, existing whenever they say it does."⁷ Acute pain in the postoperative setting is present in a surgical patient because of a preexisting disease, the surgical procedure, or a combination of the two.⁹ The inadequate treatment of acute postoperative pain has been recognized as a significant cause in the delay of hospital discharge and prolonged recovery time in surgical patients.^{3, 10, 11} Postoperative pain also increases morbidity and delays returning to normal living.¹² Additionally, unrelieved pain causes a rise in the body's sympathetic response that leads to a rise in the heart rate and increases oxygen consumption and overall cardiac workload.¹³

In today's operating rooms and post-anesthesia care units, there is a severely undertreated patient population in reference to postoperative pain management. This population includes the individuals with an active addictive disease or a history of addictive diseases.¹⁴ A social stigma exists that addiction is a choice, however, addiction is a disease.¹⁵ A disease is defined as having an etiology, signs, symptoms and causes a specific illness to the body.¹⁶ Addiction is a chronic,

relapsing and treatable disease that is characterized by a lack of control over consumption and compulsive use despite harmful consequences.⁴ Addiction also causes chronic mental illnesses and chemical changes in the patient's brain.

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utilized, the assessment must be done at regular intervals, and it must be well-documented to be effective.

The pain scales used in most settings help to provide accurate pain level assessment. However, all of these scales are very difficult to use in the acute postoperative phase of patient care due to the patient's altered level of consciousness caused by the anesthetic medications used intraoperatively.¹³ In addition to the multitude of assessment scales used to assess a patient's pain level, other factors should also be considered. A patient's preoperative analgesic use (or substance abuse), pain manage-

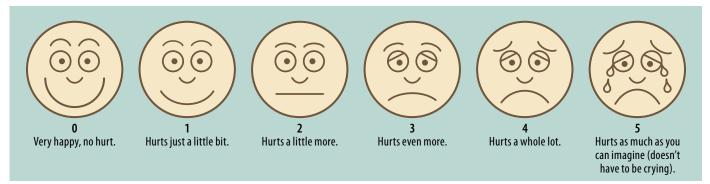
> ment history, preoperative patient education and site of operation are a few of these considerations.¹⁷ All of these factors play an important role in the way pain is perceived and also how pain is communicated by the patient.^{3, 13, 17} In most perioperative

Addiction's etiology originates in a section of the midbrain called the mesolimbic dopamine pathway. When stimulated by drugs of abuse, such as opioids, this center releases the brain's own endogenous endorphins. These endorphins are linked to the profound, euphoric feeling associated with drug intoxication. This feeling is so reinforcing that patients will seek to repeat using the drug despite dire consequences to their health and social life.^{7, 15} Thus, it can be deduced that addiction's etiology is the stimulation of the dopamine pathway by drugs of abuse, and its signs and symptoms are the destructive behaviors that addicts often exhibit.

Perioperative pain management for the patient with an opioid addiction history must begin with a thorough preoperative assessment of the patient. Proper preoperative assessment is the first and most important step in proper postoperative pain management.⁹ Many pain assessment tools are available to clinicians, including numeric scales, visual analog scales and picture scales. Regardless of which assessment tool is practice settings, a patient's pain level is assessed preoperatively by a registered nurse with a numeric scale that ranges from 0 to 10. Although having a standardized pain scale is a positive attribute for obtaining continuity of care, it seems that the particular scale in use may not be completely effective. A more objective approach in the acute postoperative phase may be appropriate until the sedative effects of the anesthesia medications decrease.^{13,17}

Use of the numerical scale is neither appropriate nor adequate for the acute postoperative setting. Clinical observations of the patient's appearance, such as sweating, sighing and the inability to move may indicate a patient in pain. Other clinical objective observations, such as an elevated blood pressure, elevated heart rate and a lack of the ability to take a deep breath may also indicate pain in the postoperative patient.^{13,} ¹⁷ In this regard, continuing education is needed in the perioperative setting. Proper training on clinical objective observations is required to adequately assess the sympathetic responses to pain that patients experience in the acute postoperative setting.^{11, 13, 17}

The assessment of pain in the acute postoperative phase of patient care is further complicated when the patient has a history of opioid addiction. This issue may, in part, be due to the preconceptions about the addictive behavior in this group of patients by caregivers and the reluctance of these patients to reveal their discomfort for fear of being judged and discriminated against.^{4, 7, 18} Patients with an addictive disease and pain have the right to be treated with dignity, respect and the same quality of pain assessment pain score, but say they are feeling well overall. This answer may be viewed by the practitioner as drug-seeking behavior when in fact studies have shown that recovering addicts may have a lower overall tolerance for pain due to chemical changes in the brain caused by the drug abuse.^{7,12} Because of these misconceptions, a more objective approach, as suggested by the World Federation of Society of Anesthesiologists, may be particularly relevant in such a situation.¹³ If the patient continually scores his pain high on a numeric scale, the practitioner may be reluctant to administer needed pain medication because he feels that this



Pain faces scale

and management as all other patients. Thus, all patients who are admitted into the post-anesthesia unit must have their pain assessed and treated with the same resilience. Health care professionals are ethically bound to manage pain and provide care to all patients, including those patients known to have an active addiction or a history of an addictive disorder.^{4, 19} With the standard of practice at many facilities utilizing the numeric pain assessment tool, the addicted patient is treated no differently than a patient without a history of an addictive disease. Therefore, the pain management is inadequate, being directly related to the assessment tool in use.

Another consideration in evaluating this numeric assessment tool is that the treatment is subjective, since an elevated pain score may be viewed by the practitioner as a drug-seeking behavior rather than actual pain.^{7, 19} Patients with a history of opioid addiction often report high pain scores regardless of their overall condition.¹² For example, they may report a high is simply drug-seeking behavior and not actual pain. Furthermore, the patient may be reluctant to admit he is in pain and give a lower pain score than is appropriate for fear of being judged by the practitioner. The patient may also have exaggerated beliefs that even a small amount of opioids introduced into his system may cause a relapse.⁷ With these findings, it seems that the assessment of postoperative pain needs to encompass not only the physical aspect, but also the emotional and psychological aspect. It should be based on objective findings rather than the subjective assessment tools currently in use.

One change that will help to ensure adequate postoperative pain management for the patient with a history of opioid addiction is to obtain a history of substance abuse in the preoperative assessment. A full history and physical, including the patient's drug history, recovery history and participation in a 12-step program, such as Alcoholics Anonymous or Narcotics Anonymous, should be obtained.⁵ Currently, many facilities do not include questions on the preoperative assessment form relating to drug abuse history. After a detailed drug and recovery history is obtained, it can be determined whether or not the patient would like to consult a pain management specialist or an addictionologist. These specialists would follow the patient throughout the perioperative experience.⁷

The patient should be informed of the many nonopioid analgesic techniques that are available to them. The patient should also be reassured that these methods will be used fully before opioids are considered.⁵ For a patient who is recovering

from an opioid addiction, the relief of knowing that they are being well taken care of and that they are not being judged will reduce the amount of tension and anxiety they have. This method has been shown to be an effective pain-management tool

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that is experienced during the perioperative setting.^{12, 21, 22} The opioid-tolerant patient will quickly enter withdrawal with a sudden decrease in the amount of opioids in his system due to not receiving the necessary doses. By maintaining the normal serum opioid level for the patient during and after the procedure, the practitioner can avoid this event. By addressing this issue, anxiety and tension, which potentially could complicate perioperative pain management and delay the patient's surgical recovery, can be avoided. Withdrawal, if not properly medically managed, can be life threatening.²¹ Both situations can be

> avoided if a complete substance-abuse history is obtained and the plan of care is altered preoperatively.

Planning for postoperative pain management in the substance abuse patient is vital in his or her postoperative experience. Not all

solely by itself.⁵ Many alternative pain treatment modalities are currently available, including epidural blocks, local and regional anesthesia, NSAIDs and local pain pumps. These methods constitute a multi-modal approach to analgesia. This approach is proven to be the best practice by many studies.^{4, 5, 12, 20}

If the patient is actively abusing opiods or alcohol, the preoperative assessment will play a different role in the postoperative management of pain. Every patient who is opioid dependent is not necessarily obtaining the medication illegally. A population of patients exists who depend on opioids to simply perform activities of daily living because of debilitating pain from injury or illness.^{12,21} A patient who takes a large dose of opioid medication on a daily basis, prescribed or illegally, naturally has a higher tolerance for the drug. What seems to be an exuberant or exceedingly large amount of medication to the practitioner may be the normal amount for the patient or the patient's tolerance level. Therefore, this amount would be ineffective for treating additional pain

patients should be treated the same, regardless of their history of substance abuse. Additional preoperative or postoperative teaching must be done for this specific patient population. It is shown that patients who are well-educated on their upcoming experience complain of less pain postoperatively than patients who are unaware of the experience they are about to encounter.⁵ A generic preoperative education form is normally given to all patients in most facilities with orders that may include, "nothing by mouth for eight hours before surgery, discontinue aspirin two weeks before surgery, do not wear makeup or jewelry to surgery, and shower with antibacterial soap the evening before surgery." The same is true for the postoperative education form, which may include orders such as, "take medication as prescribed, report any incident of fever above 101°F, do not remove dressings until your doctor sees you in the office, and keep extremity elevated if applicable." Neither of these educational forms do much for the patient with a substance abuse history to relieve his or her anxiety

about pain or alternate methods he or she can use for postoperative pain management.

Since higher levels of preoperative fear and anxiety have been shown to have a direct exacerbation effect on postoperative pain,¹³ it is important to take adequate measures to decrease the patient's preoperative fears with proper patient education and, if necessary, pharmaceutical and other alternative methods. The recovering addiction patient should be assured that his or her history of drug abuse will not be an obstacle regarding adequate and efficient treatment of postoperative surgical pain.⁵ Several medications can be given before surgery to help reduce postoperative pain.

Preoperative NSAID therapy has been shown to reduce postoperative inflammation and decrease pain and opioid requirements.¹² NSAIDs work by blocking the action of cyclooxygenase, thereby inhibiting the production of prostaglan-

The use of methadone to treat opioid addiction

Methadone is a rigorously well-tested medication that is safe and efficacious for the treatment of narcotic withdrawal and dependence. For more than 30 years, this synthetic narcotic has been used to treat opioid addiction.

Illegal narcotics, such as heroin, as well as opiate-based prescription pain medications, release an excess of dopamine in the body and cause users to need an opiate continuously occupying the opioid receptor in the brain, forming a physical dependence, or addiction. Methadone occupies this receptor and is the stabilizing factor that permits addicts on methadone to change their behavior and to discontinue heroin use.

Taken orally once a day, methadone suppresses narcotic withdrawal for between 24 and 36 hours. Because methadone is effective in eliminating withdrawal symptoms, it is used in detoxifying opiate addicts. It is, however, only effective in cases of addiction to heroin, morphine, and other opioid drugs, and it is not an effective treatment for other drugs of abuse.

Methadone reduces the cravings associated with heroin use and blocks the high from heroin, but it does not provide the euphoric rush. Consequently, methadone patients do not experience the extreme highs and lows that result from the waxing and waning of heroin in blood levels. Ultimately, the patient remains physically dependent on the opioid, but is freed from the uncontrolled, compulsive and disruptive behavior seen in heroin addicts.

Withdrawal from methadone is much slower than that from heroin. As a result, it is possible to maintain an addict on methadone without harsh side effects. Many patients require continuous treatment, sometimes over a period of years.

Methadone maintenance treatment (MMT) provides the heroin addict with individualized health care and medically-prescribed methadone to relieve withdrawal symptoms, reduces the opiate craving and brings about a biochemical balance in the body. Important elements in heroin treatment include comprehensive social and rehabilitation services.

Availability of treatment

As of 1999, about 20 percent of the estimated 810,000 heroin addicts in the United States receive MMT. At present, the operating practices of clinics and hospitals are bound by federal regulations that restrict the use and availability of methadone. These regulations are explicitly stated in detailed protocols established by the U.S. Food and Drug Administration (FDA). Additionally, most states have laws that control and closely monitor the distribution of this medication.

In July 1999, the US Department of Health and Human Services released a Notice of Proposed Rulemaking (NPRM) for the use of methadone. For the first time in more than 30 years, the NPRM proposes that this medication take its rightful place as a clinical tool in the treatment of the heroin addict. Instead of its use being mandated by regulations, programs will establish quality assurance guidelines and have to be accredited. The proposed new system will allow greater flexibility by the treating physician and ensure appropriate clinical management of the patient's needs. This proposed change in policy would eliminate most of the current regulations and allow greater clinical discretion for treatment by the physician. Accreditation establishes a clinical standard of care for the treatment of medical conditions. In the foreseeable future, clinic and hospital programs would be accredited by a national and/ or state accrediting body. Responsibility for preventing the diversion of methadone to illicit use will remain with the Drug Enforcement Administration.

dins. Prostaglandins are a principle substance that facilitates pain impulses traveling from the site of injury to the brain.⁷ The reduction of prostaglandins ultimately decreases the patient's pain. A detailed pre-operative assessment should be done to assure that NSAID therapy is not contraindicated by preexisting disease processes or anticoagulation therapy.⁵ Steroidal treatment has also been shown to relieve postoperative swelling by reducing tissue concentrations of inflammatory mediators, such as prostaglandins, thus decreasing the postoperative pain.^{7, 12, 23} Research also indicates that a 0.2 milligram Clonodine patch, applied preoperatively, may decrease anxiety by directly lowering the amount of epinephrine produced by the patient's adrenal glands, thereby decreasing the patient's overall anxiety.^{5, 12, 21, 23}

Former addicts who have been in recovery for a considerable length of time may be familiar with alternative methods of relaxation. These

Is it safe?

Like any controlled substance, there is a risk of abuse. When used as prescribed and under a physician's care, research and clinical studies suggest that long-term MMT is medically safe. When methadone is taken under medical supervision, longterm maintenance causes no adverse effects to the heart, lungs, liver, kidneys, bones, blood, brain or other vital body organs. Methadone produces no serious side effects, although some patients experience minor symptoms such as constipation, water retention, drowsiness, skin rash, excessive sweating and changes in libido. Once methadone dosage is adjusted and stabilized or tolerance increases, these symptoms usually subside.

Methadone is a legal medication produced by licensed and approved pharmaceutical companies using quality control standards. Under a physician's supervision, it is administered orally on a daily basis with strict program conditions and guidelines. Methadone does not impair cognitive functions. It has no adverse effects on mental capability, intelligence, or employability. It is not sedating or intoxicating, nor does it interfere with ordinary activities such as driving a car or operating machinery. Patients are able to feel pain and experience emotional reactions. Most importantly, methadone relieves the craving associated with opiate addiction. For methadone patients, typical street doses of heroin are ineffective at producing euphoria, making the use of heroin less desirable.

Benefits

Evidence shows that continuous MMT is associated with several other benefits.

- MMT costs about \$13 per day and is considered a cost-effective alternative to incarceration.
- MMT has a benefit-cost ratio of 4:1, meaning \$4 in economic benefit accrues for every \$1 spent on MMT.
- MMT has a significant effect on the spread of HIV/AIDS infection, hepatitis B and C, tuberculosis and sexually transmitted diseases. Heroin users are known to share needles and participate in at-risk sexual activity and prostitution, which are significant factors in the spread of many diseases. Research suggests that MMT significantly decreases the rate of HIV infection for those patients participating in MMT programs.

MMT allows patients to be free of heroin addiction. The National Institute on Drug Abuse found that, among outpatients receiving MMT, weekly heroin use decreased by 69 percent. This decrease in use allows for the individual's health and productivity to improve. Patients were no longer required to live a life of crime to support their habit, and criminal activity decreased by 52 percent among these patients. Full-time employment increased by 24 percent. In a 1994 study of drug treatment in California, researchers found that rates of illegal drug use, criminal activity and hospitalization were lower for MMT patients than for addicts in any other type of drug treatment program.

The Drug Abuse Treatment Outcome Study (DATOS) conducted an outpatient methadone treatment evaluation examining the long-term effects of MMT. The pretreatment problems consisted of weekly heroin use, no full-time employment and illegal activity. Results of the 1-year follow-up showed a decrease in the number of weekly heroin users and a reduction in illegal activity after OMT. There was no significant change in unemployment rates.

Taken from the Executive Office of the President: Office of National Drug Control Policy. Available at: http://www.whitehousedrugpolicy.gov/ publications/factsht/methadone/index.html nonpharmaceutical methods include techniques such as imagery, meditation and breathing exercises. Some patients may wish to use these methods rather than using medications preoperatively. In addition, a patient may wish to have his or her Alcoholics Anonymous or Narcotics Anonymous-appointed sponsor present throughout the operative experience. Others may also wish to hold 12-step meetings before and after the procedure to assist in their mental and spiritual wellbeing. To relieve a patient's anxiety, all efforts should be made when possible to abide by his or her wishes.¹²

In the author's current practice, the preoperative standing orders for all patients are to admin-

ister Versed, Robinul and Reglan. Versed is a benzodiazepam that reduces anxiety and causes mild sedation.⁷ While this medication is useful to reduce anxiety immediately preoperatively and is not contraindicated in opioid-addicted patients, it

does very little to address the previously-stated issues that the recovering addict patient faces. Robinul is an anticholinergic medication that has no effect on the patient's mental or emotional state. Reglan is an antiemetic and gastrointestinal stimulant that causes gastric emptying to help prevent nausea.⁷ These two medications do nothing to address the addicted patient's concerns. Improvement in perioperative practice is necessary in relation to preoperative education and medication orders for this specific population of patients to address their needs.

In patients with no history of substance abuse, opioids are the first line medications used for postoperative pain management in most facilities. In the majority of hospitals, the combination of opioids with the above-mentioned standard preoperative medication orders seems to be satisfactory. Unfortunately, this is not the case for patients with a history of substance abuse. Studies show that reintroducing opioids into a recovering patient's system will activate the reward and reinforcement center of the brain involving the ventral tegmental area of the midbrain, where dopaminergic neurons originate. This result causes severe drug craving and seeking behaviors to begin, therefore restarting the addictive cycle over again. For the recovering addict in the acute postoperative phase, it is important to make use of a multimodal analgesic approach.^{5, 12, 15} As previously mentioned, local anesthetics, regional and epidural blocks, NSAIDs, prostaglandin inhibitors and local postoperative pain pumps are many of the resources available to practitioners. Local anesthetics, regional and epidural blocks help to break the initial pain response

> felt by patients. Some medications, such as 0.25 percent -0.75 percent Bupivicaine, last as long as three hours. Studies have supported the theory that opioid consumption can be brought to a minimum and maybe even eliminated from use with the

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> proper advent of local anesthetics.^{7,24} In the case of epidural usage, the epidural catheter can be left intact until several hours after the procedure to ensure comfort for the patient in the acute postoperative phase.^{7, 12, 23, 24, 25}

> Evaluation of the effects of the pain management therapy, whether it is a nonpharmacological or pharmacological method, should be performed at regular intervals. It is much easier to control pain if it is stopped before it begins rather than try to "play catch up." Once the sympathetic response to the pain stimulus is initiated, it is harder to control and eventually halts the effects of the stimulus. Hence, the objective pain assessment methods, as discussed earlier and suggested by The World Federation of Society of Anesthesiologists, should be implemented.¹³

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Pain management for patients with a substance abuse history

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Telephone

- 1. Health care workers should be cautious when prescribing opioids to
- a. Transplant recipients
- b. Cardiac patients
- c. Diabetic patients
- d. Recovering addicts
- 2. One component of pain is _
- a. Physical c. Pain scale
- b. Pre-existing d. Opioids
- 3. The emotional components of pain include:
- a. Anger
- b. Sadness
- c. Depression
- d. All of the above
- 4. Acute pain in postoperative surgical patients is due to:
- a. Emotional distress
- b. Preexisting disease
- c. Surgical procedure
- d. A combination of B and C

leads to a rise in heart rate, increased oxygen consumption and overall cardiac workload.

- a. Opioid prescription
- b. Unrelieved pain
- c. Arterial blockage
- d. Intoxication

- 6. _____is a chronic, relapsing and treatable disease characterized by lack of control over consumption and compulsive use despite harmful consequences.
- a. Addiction c. Crohn's
- b. Diabetes d. Arthritis
- 7. The most important step in proper postoperative pain management is:
- a. Administration of prescription drugs
- b. Maintaining the dopamine pathway
- c. Proper preoperative assessment
- d. Understanding and treating a patient's addiction
- 8. An example of a pain assessment tool is a:
- a. Numeric Scale c. Picture scale
- b. Visual analog scale d. All of the above
- A patient's altered level of consciousness in the acute postoperative phase of care due to intraoperative anesthetics makes it hard to successfully administer:
- a. An IV drip c. A pain assessment
- b. Oral analgesics d. All of the above

10. Physical indications of pain in the acute postoperative setting include:

- a. Sweating
- b. Elevated heart rate
- c. Trouble moving/taking deep breaths
- d. All of the above

Pain management for patients with a substance abuse history		а	b	C	d		а	b	C	d
Certified Member Certified Nonmember	1					6				
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Mark one box next to each number. Only one correct or best answer can be selected for each question.

edits.

- 11. One way to help ensure postoperative pain management for a patient with a history of opioid addiction is:
- a. Obtain a preoperative substance abuse history
- b. Consult an addictionologist
- c. Administer frequent pain scale tests
- d. Begin a preoperative pain management regimen

12. Which of the following is *not* an alternative pain treatment?

- a. Electro-shock therapy
- b. Local and regional anesthesia
- c. Epidural blocks
- d. Local pain pumps

13. Postoperative fears for opioid-dependent patients may include:

- a. Being judged by the care giver
- b. Suffering a relapse into drug use
- c. Not receiving enough pain medication
- d. All of the above

14. Blocking the action of cyclooxygenase and inhibiting prostaglandin production can be accomplished with:

- a. Steroidal treatment
- b. A Clonodine patch
- c. NSAID therapy
- d. All of the above

15. ________is a synthetic narcotic used to treat opioid addiction. a. Heroin c. Methadone

b. Clonodine d. Prednisone

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Pain management for patients with a substance abuse history

16. Methadone is used in the treatment of addic-

- tion to:
- a. Opiates
- b. Alcohol
- c. Methamphetamines
- d. All of the above

17. Side effects of Methadone use include:

- a. Impairs cognitive functions
- b. Debilitating drowsiness
- c. Liver damage
- d. Methadone has no serious side effects

18. Opiates provide a flood of ______, which causes the euphoric high associated with drug use.

- a. Epinephrine
- b. Dopamine
- c. Endorphins
- d. Morphine

19. The preoperative assessment for a substance abuser should include:

- a. The patient's drug history
- b. The patient's recovery history
- c. A full physical
- d. All of the above

20. Patients who take opiates in large doses have

- a higher _____
- a. Pain threshold
- b. Drug-seeking behavior
- c. Tolerance
- d. All of the above

	а	b	c	d		а	b	c	d
11					16				
12					17				
13					18				
14					19				
15					20				

Mark one box next to each number. Only one correct or best answer can be selected for each question.