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Review & Commentary

Pain Management in Trauma Patients

ABSTRACT

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Trauma is a major cause of mortality throughout the world. In recent years, major advances have been made in the management of trauma, the end result of which has been reduced mortality and enhanced function. One of these areas is pain control. Improved pain management has not only led to increased comfort in trauma patients, but has also been shown to reduce morbidity and improve long-term outcomes. This review focuses on the treatment of pain in the setting of acute injury and on pain management in trauma patients who go on to develop chronic pain. Emphasis is placed on pharmacologic interventions, invasive and noninvasive pain management techniques, analgesia in challenging patients, and pain control in commonly encountered trauma conditions.

Key Words: Pain Management, Trauma Patients, Chronic Pain, Pharmacologic Interventions

In addition to the cost in lives, productivity, and money, trauma exacts a steep toll on patients in the form of physical suffering and mental anguish. In a study by Whipple et al.[1] assessing pain treatment in 17 patients with multiple trauma wounds, whereas 95% of house staff and 81% of nurses reported adequate analgesia, 74% of patients rated their pain as either moderate or severe. There are multiple reasons for poor pain management in trauma patients, including under-appreciation of pain, excessive concern about hemodynamic instability and respiratory depression, and an unfounded fear of addiction. Yet to properly manage trauma, it is incumbent to aggressively treat pain, for the ramifications of inadequate pain control are more than just psychological.

Over the past two decades, researchers have discovered that the persistence of severe, inadequately treated pain can lead to anatomic and physiologic

changes in the nervous system.[2] The ability of neural tissue to change in response to repeated incoming stimuli, a property known as neuroplasticity, can lead to the development of chronic, disabling neuropathic pain when acute pain is poorly treated.

The stress response after multiple trauma is far greater than that after elective surgery. This response, which includes cytokine and acute phase reactant release; elevated levels of catecholamines, cortisol, growth hormone, and adrenocorticotropic hormone; activation of the renninangiotensin system; impaired coagulability; and an altered immune response, accounts for a large portion of the mortality in trauma patients.[3] In several studies, inadequately treated acute pain has been shown to increase this response, resulting in higher morbidity.[4,5]

Finally, untreated pain can potentiate the adverse effects trauma has on normal physiologic phenomena such as ventilation, hemodynamic stability, and gastrointestinal and renal function. Further compromise of these already impaired processes can result in increased morbidity and mortality. Because most of the studies involving trauma patients are based on iatrogenic trauma (i.e., surgery), care must be taken when extrapolating these findings to patients involved in accidents. Nevertheless, it is becoming increasingly apparent that the proper treatment of pain is essential to optimize outcomes in trauma victims.

ANALGESIC AGENTS

Acetaminophen. Acetaminophen and its metabolic predecessor, phenacetin, exert their analgesic effects via the inhibition of cyclo-oxygenase (COX), the rate-limiting enzyme in prostaglandin synthesis. Because acetaminophen is a nonacidic phenol derivative, it readily crosses the blood-brain barrier, where prostaglandin inhibition produces analgesia and antipyresis, with minimal anti-inflammatory effects. The neutral pH and low affinity for plasma proteins of acetaminophen and phenacetin does not lend itself to accumulation in the gastrointestinal tract, blood stream, and collecting ducts of the kidney. As such, in therapeutic doses, nonacidic COX inhibitors are devoid of renal, platelet, and gastrointestinal toxicity. Acetaminophen can be given orally or rectally at a maximal dose of 65 mg/kg/day. Although acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDS) are usually not sufficient by themselves to treat severe pain, their safety profile in proper dosing regimens makes them valuable adjunct medications in trauma patients. Dosing acetaminophen by age may underestimate the analgesic requirements in pediatric patients.

NSAIDS. NSAIDS are powerful inhibitors of COX and a first-line treatment for many painful conditions. Originally thought to act almost exclusively in the periphery, it is now known that NSAIDS also inhibit prostaglandin synthesis in the central nervous system (CNS). The main drawbacks to NSAIDS are their low analgesic ceiling, inhibition of platelet function, and renal and gastrointestinal toxicity. Recently, a new class of NSAIDS has been introduced that selectively inhibit the COX-2 isoenzyme, the inducible isoform involved in inflammation and pain. Preservation of the constitutive COX-1 enzyme significantly reduces the risk of bleeding and gastrointestinal ulceration. New NSAIDS under investigation inhibit 5-lipo-oxygenase (LOX) and COX, and are referred to as dual LOX/COX inhibitors.

Opioids. In light of their long and unparalleled record of providing pain relief throughout the centuries, opioids are the gold standard for treatment of severe pain. For many patients with intense, unremitting pain, opioids, because of their high ceiling effect, are the only group of drugs capable of providing relief from suffering.

Opioid analgesics exert their actions through inhibition of target cell activity. Mediating these effects are three endogenous opioid receptors: mu, delta, and kappa. Peripheral opioid binding sites have also been identified, which require inflammatory mediators for their activation. The significance of these peripheral receptors is not fully understood. The predominant analgesic sites of opioids are believed to reside in the CNS, including the brainstem, thalamus, forebrain, and spinal cord. Some proposed mechanisms of opioid analgesia include: membrane hyperpolarization via activation of potassium channels; suppression of voltage-gated calcium channels, resulting in the diminished terminal release of neurotransmitters; and receptor-mediated inhibition of adenylate cyclase.

Opioids selectively relieve pain and the affective response to nociception; they have no effect on motor or other sensory modalities. Patients will often say that they still have pain, but feel more comfortable. Opioids sometimes produce euphoria or dysphoria, which is more common when short-acting opioids are administered or when the drugs are used for recreational purposes. Although useful analgesia is seen without loss of consciousness, drowsiness is common, and overdose can lead to unconsciousness.

In addition to oral, parenteral, and neuraxial administration, opioids can also be given rectally, transdermally, and transmucosally in the form of fentanyl lollipops. Because it avoids first-pass hepatic metabolism, the onset of analgesia is faster with transmucosal administration than with the oral route, and it can be used in patients who may receive nothing by mouth.

ADJUVANTS

Ketamine. Ketamine is an arylcyclohexylamine congener of phencyclid-

ine that is usually employed in medicine as a general anesthesia induction agent. Whereas the effects of ketamine on neural transmission are less well described than other anesthetics, it has been reported to act antagonistically at muscarinic receptors and as an agonist at sigma (opioid) receptors.[6]

Ketamine's ability to noncompetitively block N-methyl-D-aspartate (NMDA) receptors has generated great interest in pain research. In both animal and human studies, the stimulation of NMDA receptors has been implicated in central sensitization and opioid tolerance.[7] When administered parenterally, ketamine produces a "dissociative" state within 1 min that is accompanied by amnesia and profound analgesia.

The main advantages ketamine enjoys over opioids are better preservation of spontaneous ventilation and airway reflexes and stimulation of the cardiovascular system. Adverse effects include increased secretions, agitation on emergence, and hallucinations, the latter of which can be minimized by the concomitant use of benzodiazepines. Although the lack of a readily available oral formulation and the high prevalence of psychomimetic effects limit its use for background pain, ketamine is an ideal agent for painful procedures such as wound debridements and closed reductions.

Local Anesthetics. Although lidocaine is well known for its pain-relieving properties as a local anesthetic (LA), its use in trauma is limited because of fear of toxicity. This may be especially true in burn patients.[8] Rare cases of toxicity have been observed with topical application to mucosal membranes, resulting in rapid absorption,[9] and with lidocaine gel applied to burns in children, leading to seizures.[10] Despite these rare occurrences, topical lidocaine may provide useful analgesia in traumatic conditions such as burns. For instance, Brofeldt et al.[11] demonstrated that 5% topical lidocaine cream applied to contained burns (≤28% burn surface area) offered substantial pain relief for 4–6 hrs, with no systemic side effects. In normal circumstances, topical application differs from transdermal administration in that systemic effects are insignificant.

The use of lidocaine intravenously can also be considered in treating trauma pain. In a study by Jonsson et al.,[12] an intravenous lidocaine bolus of 1 mg/kg followed by a 3-day continuous infusion of 40 μg/kg/min was reported to be safe and effective in treating burn pain. No systemic side effects to lidocaine were observed during the infusion period. A study in animals by the same group concluded systemic or topically administered LAs can also improve dermal perfusion in the burned area.[13] Lidocaine's mechanism of action in burn pain remains elusive, although its ability to depress conduction of painful afferent signals, suppress ectopic discharges by injured nerves, inhibit dorsal horn transmission, and reduce inflammation may all contribute to its therapeutic effects.[14,15] In patients who respond to systemic lidocaine, the oral analog mexiletine can provide comparable therapeutic effects.[16] Interestingly, a lidocaine infusion may assist in treating trauma-related anxiety through its ability to induce a euphoric state.

Antidepressants. Tricyclic antidepressants (TCAs) can reduce pain, alleviate depression, and facilitate sleep in patients with trauma injuries. Randomized, controlled trials provide strong evidence that TCAs can treat neuropathic pain, with their analgesic effect being independent of their antidepressant action. Low doses of TCAs reduce the need for opioids while enhancing their analgesic effects.[17]

Studies have found low levels of CNS neurotransmitters to be associated with both depression and pain.[18] Because TCAs prevent the reuptake of serotonin and norepinephrine in the CNS, they may promote the effects of descending, antinociceptive pathways, thus reducing trauma pain.

Anticonvulsants. Drugs such as phenytoin and carbamazepine suppress spontaneous neuronal firing in the brain, thus achieving their anticonvulsant effects. Newer agents such an gabapentin, topiramate, lamotrigine, tiagabine, and oxcarbazepine exhibit unique and sometimes overlapping mechanisms of action in treating convulsions and, more recently, neuropathic pain.[19] Several of these agents also suppress peripheral nociceptive neuronal firing and may therefore be of therapeutic use in trauma-related pain. Because neuropathic pain commonly occurs in patients with healed burns, anticonvulsants may have special application in this population.

Clonidine. Clonidine is a lipid-soluble alpha-2 adrenergic agonist with analgesic and sedative properties that may be useful both in trauma pain and as a preanesthetic medication in adults and children. Studies have shown clonidine to reduce perioperative analgesic requirements, prolong the duration of LAs, and enhance opioid analgesia.[20,21] Routes of administration include oral, intravenous, transdermal, intramuscular, and neuraxial.

Hemodynamically unstable patients should not receive clonidine because of the risk of hypotension. Alpha-2 adrenergic agonists may have a role in reducing trauma pain as sole agents or in concert with opioids or LAs, given the known synergism between the drugs.

Benzodiazepines. This class of medications lacks analgesic properties but promotes sedation, muscle relaxation, and anxiolysis, the latter of which can lower psychological fea-

TABLE 1
Equianalgesic doses of opioids (in milligrams)

	Oral	Parenteral	Epidural	Intrathecal	Water Solubility
Morphine	300	100	10	1	High
Hydromorphone	60	20	2	0.2	Intermediate
Meperidine	3000	1000	100	10	Low
Fentanyl	—	1	0.1	0.01	Low
Sufentanil	—	0.1	0.01	0.001	Low

tures of pain. Although many researchers have shown that anxiety exacerbates pain, the data for this supposition is conflicting.[22] When a benzodiazepine is used in conjunction with opioids, the opioid dose required to produce analgesia is reduced. For example, Patterson et al.[23] found that the addition of low-dose lorazepam to standard opioid therapy in burn patients resulted in a significant reduction in pain scores. Benzodiazepines produce anterograde amnesia, an effect that can improve a patient's perception of trauma pain. Patients most likely to benefit from anxiolytics are those with high anxiety and high pain scores.

Midazolam and diazepam are first-line agents for systemic sedation. Compared with diazepam (T1/2 *B* 24–60 hrs), midazolam offers a shorter duration of action (T1/2 *B* 2–3.5 hrs, duration 60–90 min). Children may tolerate oral or nasal midazolam (0.4–0.5 mg/kg) better than parenteral routes, although the clinical effects are less predicable.

Entonox. Inhaled nitrous oxide and oxygen, usually in 50:50 mixtures, can provide safe and effective analgesia and anxiolysis without loss of consciousness for moderately painful trauma-related procedures.[24] Typically, it is self-administered by an awake, cooperative patient via a mask or mouthpiece. Like patient-controlled analgesia (PCA), patients control their intake with a demand-valve device. The demand valve permits patients to discontinue gas flow when somnolence occurs. Critically ill and uncooperative patients are poor candidates for this treatment.

Entonox produces analgesia and anxiolysis about 20 secs after inhalation, with peak effects occurring within 2 mins. The gas smells sweet and can cause mild excitability, drowsiness, nausea, or paresthesias. Cardiovascular side effects are minimal in concentrations of 50% nitrous oxide and oxygen. Entonox should be avoided in patients with altered sensorium, bowel obstruction, pneumothorax, head injury, chronic obstructive pulmonary disease, decompression sickness, or air embolism.

Corticosteroids. Corticosteroids are useful for treating trauma pain induced by peripheral nerve injuries, soft-tissue damage, bone metastases, nerve compression, visceral distension, increased intracranial pressure, and spinal cord injury. Typical agents include prednisone, methylprednisolone, hydrocortisone, and dexamethasone.

PAIN RELIEVING PROCEDURES

Pharmacologic Interventions

Epidural Analgesia. Epidural analgesia is achieved by the introduction of analgesics into the epidural space. Medications injected epidurally act directly on spinal nerves and receptors in the spinal cord via diffusion across the dura and into the cerebrospinal fluid.

The most frequently used medications for epidural analgesia are LAs. LAs administered neuraxially or during peripheral nerve blocks arrest nerve conduction via the blockade of sodium channels, the sentinel event in the depolarization of neurons. As such, LAs block the transmission of all nerve fibers, not just the A delta and C fibers responsible for pain. Side effects of epidural LA infusions include hypotension from sympathetic blockade and muscle weakness.

The second most commonly used medications for epidural analgesia are opioids, which act via mu, kappa, and delta receptors in the substantia gelatinosa of the spinal cord. One advantage epidural opioids hold over LAs is the lack of autonomic and motor blockade. The ten-fold reduction in equianalgesic doses of opioids between the epidural and intravenous routes translates to a reduced prevalence of certain side effects such as sedation and constipation during neuraxial administration (Table 1). Other opioid side effects such as pruritus are more common with the neuraxial route.[25] A major limitation of epidural analgesia is that the spread of medication, and hence analgesia, is segmental. Thus, the large volumes required to cover extensive injuries can lead to significant systemic blood levels and side effects. For epidural narcotics, hydrophilic drugs such as morphine exhibit greater segmental spread and result in better pain relief than lipid-soluble drugs like fentanyl. Unfortunately, greater rostral spread also results in a higher prevalence of side effects.[26] Contraindications to neuraxial analgesia include coagulopathy, local in-

TABLE 2
Standard patient-controlled analgesia settings for frequently used opioids

	Morphine	Hydromorphone	Fentanyl	Meperidine
Concentration	1 mg/ml	0.2 mg/ml	10 μg/ml	10 mg/ml
Demand dose	1 mg	0.2 mg	10 μg	10 mg
Basal rate	0–1 mg	0–0.2 mg	0–10 μg	0–10 mg
Lockout interval	6–10 mins	8–12 mins	6–10 mins	6–10 mins

In patients with renal failure, meperidine and morphine should be used with extreme caution; hydromorphone and fentanyl are considered "safe" opioids in these patients.

fection overlying the needle insertion site, generalized sepsis, severe hypovolemia, progressive neurologic deficit, and elevated intracranial pressure.

Regional Anesthesia. In the trauma patient with crush injuries, fractures, and burns limited to a limb, nerve blocks can provide an attractive pain management alternative to systemic narcotics. For upper limb injuries, these techniques include interscalene, supraclavicular and infraclavicular, and axillary nerve blocks. Interscalene block provides the most reliable anesthesia for shoulder pain, supraclavicular and infraclavicular blocks for injuries sustained below the shoulder and above the elbow, and axillary block for pain originating in the hand and forearm.[27]

In patients with unilateral lower limb pain who are not candidates for epidural blockade, lumbar plexus and sciatic nerve blocks can provide excellent pain relief. The sensory innervation to the anterior thigh is through three nerves, the femoral, obturator, and lateral femoral cutaneous. These nerves can be blocked via an anterior approach, the "three-in-one" lumbar plexus block just below the inguinal ligament, or through a posterior approach, the psoas compartment block. The sciatic nerve provides innervation to the posterior thigh and most of the lower leg. There are several different techniques that can be used to block the sciatic nerve, but the most commonly used one is the posterior "classic" approach, midway between the sacral hiatus and greater trochanter.[28] For peripheral nerve blocks, catheters can be inserted to provide continuous LA infusions.

PCA. PCA is an extremely popular opioid delivery system in patients with acute trauma. The safety mechanism of the PCA delivery system lies in the lockout period, a preset interval whereby the patient is "locked out" from receiving demand-dose medication delivery. If a patient self-administers a dose that causes sedation, he or she will not push the button again until the untoward side effect dissipates.

In acute pain studies performed on postsurgical patients, the outcomes comparing PCA with intermittent intravenous or intramuscular narcotic boluses are mixed, although the majority tend to show improved analgesia and decreased opioid consumption in patients receiving PCA.[29] With regard to the utility of a basal rate, the study outcomes are also mixed. However, because most show no improvement in pain relief but increased narcotic consumption when basal rates are administered,[30,31] it may be prudent to begin PCA in opioid-naïve patients with demand dosing only (Table 2). Recently, the addition of low-dose ketamine to traditional opioid PCA regimens has been found to be beneficial in some patients.[32]

Nonpharmacologic Interventions

Transcutaneous Electrical Nerve Stimulation. Transcutaneous electrical nerve stimulation (TENS) is a noninvasive technique that may be a useful adjunct in reducing pain in trauma injuries. Studies have documented the successful use of TENS in treating postoperative pain, pain associated with rib fractures, and in burn pain.[33–36]

As a sole analgesic, Oncel et al.[35] showed that TENS was more effective than NSAID or placebo in controlling pain in patients with uncomplicated rib fractures. TENS may also reduce analgesic requirements in conjunction with other analgesics, as confirmed by studies of postoperative opioid use in patients receiving TENS.[33] In addition to its analgesic effects, Sloan et al.[36] demonstrated improvements in peak expiratory flow rates and arterial oxygen concentration in patients with multiple rib fractures receiving TENS. TENS is best utilized in trauma pain as an adjunctive analgesic similar to NSAIDS.

Hypnosis. Applied to trauma, hypnosis entails the use of suggestions to alter the perception or cognition of painful events. The hypnotherapist offers suggestions for dissociation from severe pain and unpleasantness, thus producing comfort. The nature of the pain is not pertinent to the success of hypnosis because the goal focuses on reduced suffering. In fact, evaluating a patient's understanding and expectations about pain is crucial to the hypnotherapist. Both adult and pediatric patients suffering from burn pain, postoperative pain, and

pain due to medical procedures may benefit from hypnosis.[37–40]

Acupuncture. Substantial data support the efficacy of acupuncture in treating painful syndromes. Studies implicate the CNS, peripheral nervous system, endorphins, and monoamine neurotransmitters as mechanistic processes in inhibiting pain. One clinical investigation on burn patients showed that auricular acupuncture-like TENS significantly reduced the pain after dressing changes, wound debridement, and other wound care compared with placebo.[41] Although numerous studies report that acupuncture can provide from 50% to 80% short-term relief from painful conditions, larger, better-designed clinical trials are needed to assess efficacy.[42]

Psychological Interventions. Fear, anxiety, and depression account for substantial psychological stressors in patients experiencing trauma pain. Prolonged, severe anxiety stemming from uncontrolled pain after traumatic injury has even been deemed to be a cause of posttraumatic stress disorder.[43] As such, psychological techniques can serve as adjuncts to other pain-relieving modalities in controlling pain. Both cognitive and behavioral approaches can modulate the emotional dimension of acute pain.

Cognitive interventions permit patients to view inner thoughts as modifiable behavior, which can alter pain perception. Avoidance and distraction strategies incorporate imagery as a tool for modulating painful events. For example, a patient can envision himself lying on a comfortable beach, free of pain, or perform arithmetic problems during painful procedures. Reappraisal approaches used in burn patients refocus thoughts on painful stimuli in a manner that restructures the input in a more positive context. For instance, unpleasant sensations during dressing changes may constitute "good pain" or a necessary part of wound healing.

Relaxation techniques can decrease sympathetic arousal through progressive muscle relaxation, controlled breathing, and visual imagery. Biofeedback monitors physiologic processes (skin temperature, blood flow, and heart rate) and "feeds back" the information to the patient using electromechanical equipment. Together, relaxation and biofeedback can be useful in decreasing pain states. Spence et al.[44] successfully used electromyographic biofeedback and relaxation techniques in patients suffering from upper limb trauma. In this study, electromyographic biofeedback, relaxation training, and a combined approach all led to significant short-term reductions in pain, anxiety, and depression. More recently, a new psychological treatment called eye movement desensitization and reprocessing has been shown to offer a rapid reduction in pain and distressing thoughts and feelings.[45]

PAIN MANAGEMENT IN DIFFICULT PATIENTS

Drug-Addicted Patients

Alcoholics. The essence of trauma injuries translates to a substantial percentage of patients addicted to alcohol and narcotics. The tolerance of alcoholic patients to alcohol is paralleled by a similar tolerance to other CNS depressant drugs. Cross-tolerance to opioids may necessitate increasing dosages in sober alcoholics. In patients with advanced liver disease, complicated alterations in drug pharmacokinetics make it difficult to predict the appropriate dosing regimen. Factors that must be considered in advanced alcoholic liver disease include reduced hepatic metabolism, decreased protein binding, an increased volume of distribution when ascites is present, and the concomitant presence of cardiomyopathy. In alcoholics receiving disulfiram, potentiation of the effects of CNS depressants may occur secondary to the ability of disulfiram to inhibit the metabolism of drugs other than alcohol. Overall, the presence of endstage alcoholic liver disease is usually associated with an increased sensitivity to and prolonged duration of action of opioid analgesics.[46]

In contrast to the chronic but sober alcoholic, the intoxicated alcoholic patient requires less opioids because there is an additive effect between alcohol and narcotics. The acutely intoxicated patient also withstands stress poorly and may be more vulnerable to regurgitation of gastric contents with the administration of intravenous analgesics.

Opioid-Addicted Patients. A disproportionately large percentage of trauma patients have a history of intravenous drug abuse,[47] yet the injuries they suffer necessitate treatment with opioids. When treating these individuals, the fundamental principle of pain management is the same as it is for other patients: pain complaints should be taken seriously and treated aggressively. Although some researchers have reported opioid addicts to have increased pain sensitivity compared with normal subjects, in one study, intravenous drug addicts were not found to complain more of pain or require larger doses of opioids than those who were not drug abusers.[48–50]

In many instances, the development of opioid cross-tolerance means intravenous drug abusers will require higher doses of analgesics to obtain similar degrees of pain relief. For patients with chronic, unremitting pain, such as those with burn injuries, long-acting opioids provide a steady state of analgesia and are associated with less euphoria and the slower development of tolerance than short-acting narcotics. Consequently, they also tend to have a lower abuse potential. The fentanyl patch has perhaps the lowest potential for abuse,

TABLE 3
Selected pediatric pain rating scales

Pain Instrument	Description
Neonates, infants, and young children	
CRIES	0–10 scale using five variables: C, crying; R, requirement for supplemental oxygen; I, increased vital signs; E, expression; S, sleeplessness
Premature Infant Pain Profile	Utilizes behavioral state, heart rate, oxygen saturation, brow bulge, eye squeeze, and nasolabial furrow to assess pain
Neonatal Facial Coding System (NFCS)	Focuses on a limited subset of facial actions
Facial Action Coding System (FACS)	Comprehensive coding system focusing on all facial actions
COMFORT Scale	Uses combined behavioral and psychophysiologic indices
Preschoolers	
Poker Chip Tool	Child evaluates pain intensity using 1–4 "poker chips" representing "pieces of hurt"
Child Facial Coding System	Codes for the presence or absence of 13 facial actions
School age	
Faces Scale	Category scale consisting of faces expressing varying amounts of distress
Oucher Scale	Variant of Faces Scale displayed in poster format, accompanied by a vertical numerical scale (0–100)
Charleston Pain Pictures	Consists of 17 cartoon pictures depicting situations with varying degrees of pain
Adolescent	
Verbal pain scores	Same as for adults
Numerical rating scales	
Visual analogue scales	

although innovative drug addicts have found methods to abuse even this.

When patients in methadone maintenance programs or those receiving long-acting opioids for chronic conditions present with trauma injuries, the long-acting medications should be continued, and PCA should be added to provide additional analgesia for the acute injury and as a means for assessing opioid requirements. In patients who may receive nothing by mouth, the long-acting opioid can be converted to a basal rate. Mixed agonist-antagonists should be avoided in opioid-dependent patients because they can trigger withdrawal. In patients with inadequately treated pain, pseudo-addiction can be misinterpreted as drug-seeking behavior.

Pediatric Patients. Studies have shown that children tend to be under-medicated after trauma or major surgery due in part to a global fear of overdose.[51,52] However, pharmacodynamic and pharmacokinetic studies support the safety of proper doses of analgesics and LAs in children. It is now the prevailing opinion that clinicians should always provide proper pain-relieving treatments, even in small children. Mounting evidence shows that adequately treating pain in children is not only safe, but can also improve outcomes.[52]

In individuals aged 1–25 yrs of age, motor vehicle accidents are the number one cause of death and serious injury. Motor vehicle accidents not withstanding, preschool children tend to have accidents inside the home, whereas school-aged kids usually sustain injuries from accidents occurring outside the home.[53] During transport from the scene of an accident, parenteral analgesics should be used in severely injured children. Intramuscular morphine (0.1 mg/kg) furnishes reasonable pain relief during undressing and mobilization. Femoral nerve blocks are easy to perform and can be used successfully in children as young as 2 yrs of age before transferring an injured child to a stretcher, operating table, or imaging table. Low-dose opioid infusions can provide needed analgesia in the preoperative period or before immobilization/reduction of fractures. Ketamine, usually in conjunction with a benzodiazepine, can also be used for pain relief before and during procedures. One caveat when treating pediatric pain is that it is crucial to give traumatized children support and reassurance to minimize fear. Even in emergency situations, relaxation methods can be employed expeditiously before initiating painful procedures.

In older children, pain can be assessed by means of the visual analog scale, a faces scale, or a physiologic and behavior scale like the Washington, DC, Pediatric Pain Scale. These instruments require little time to complete and provide a good measurement of pain in children as young as 3 yrs of age. In infants and neonates, the Neonatal Facial Coding System and COMFORT Scales can be helpful in guiding pharmacologic and nonpharmacologic pain therapies (Table 3). Once pain is assessed, an array of regional tech-

niques or analgesic medications can be incorporated. Nerve blocks may be appropriate for children both in an acute setting and before surgery. These include ilioinguinal blocks for pelvic pain, intercostal or interpleural blocks for chest trauma, and peripheral nerve blocks for limb fractures. Although nerve blocks should ideally be performed on awake patients who can communicate, in some instances, heavy sedation or even anesthesia may be necessary.

Upper limb blocks via the brachial plexus are used for laceration repairs, closed reductions, or surgery performed on the arms. In children, Dalens[54] recommends a parascalene approach that targets the crossing of the pectoralis muscle with the coracobrachialis muscle. Advantages of this approach include technical simplicity and a lower prevalence of Horner's syndrome. The recommended LA volume range for brachial plexus blocks is 0.6–0.7 ml/kg.

Femoral nerve blocks can be useful for children with fractures of the femoral shaft.[55] The typical volume is 0.2–0.3 ml/kg LA for isolated femoral nerve blocks or 0.5–0.7 ml/kg for a three-in-one block (obturator, femoral, and lateral femoral cutaneous nerve blocks). Caudal and epidural blocks are not recommended in trauma patients with lumbar spine injuries, skin damage to the sacral hiatus, or severe dehydration.

Incapacitated Patients. Patients with intellectual disabilities are at increased risk for trauma injury.[56] These patients may be unable to adequately express their pain or medical providers may inaccurately interpret their expressions of pain. Studies using the Facial Action Coding System have found this comprehensive battery of facial expressions to be both a valid and reliable indicator of pain in patients unable to adequately express themselves.[57] Painful expressions typically observed include blinking, mouth opening, eye orbit tightening, nose wrinkling, and brow lowering.

Pain assessment in patients with abnormal mental function in the intensive care unit due to depressed consciousness, ventilatory dependence, or delirium can be challenging. Patients should be examined for painful gestures or changes in baseline autonomic function. As with communicative patients, medication response (decreased blood pressure and heart rate or a reduction in painful postures) should guide opioid dosage rather than precalculated unit doses. In the acute care setting, opioids are commonly administered for analgesia and sedation, with morphine and fentanyl being most frequently used.

Epidural and intrathecal opioids should be avoided in uncooperative patients. In these individuals, a continuous intravenous opioid infusion rather than intermittent dosing is recommended. Intermittent dosing often leads to inadequate analgesia, higher peak blood levels, and increased side effects. For cooperative patients, PCA is an effective pain-relieving device. For those with disordered mentation, continuous infusions of fentanyl or morphine are preferred at doses ranging from 20 to 100 μg/hr and 2 to 8 mg/hr, respectively. Fentanyl is preferred over morphine in hemodynamically unstable individuals because of its low tendency to stimulate histamine release. Meperidine carries the risk of neurotoxicity and therefore is avoided in acute care settings. Normeperidine, meperidine's active metabolite, can produce delirium, hallucinations, psychosis, and seizures if it accumulates in renal failure or with repeated doses.

The NSAID ketorolac can be used in acute care settings in patients with depressed mental function. As a parenteral nonsteroidal analgesic, it produces none of the opioid-related side effects but can cause platelet inhibition and irritation to the gastric mucosa. Ketorolac can be administered orally, intramuscularly, or intravenously, and it is often used in conjunction with an opioid. Parenteral dosing of ketorolac should not exceed 5 days. Doses should be adjusted for low body weight, advanced age, and impaired renal function.

In delirious patients, clinicians should focus on identifying and treating the underlying cause of the problem. If sedatives are necessary, the choice should be based on the cause of the delirium (i.e., intensive care unit–related delirium can be treated with haloperidol and alcohol withdrawal with benzodiazepines); only then can proper pain assessment and treatment can be instituted.

SPECIFIC TYPES OF TRAUMA

Blunt Chest Trauma

Although the precise incidence is unknown, blunt chest wall injuries are not uncommon, with blunt thoracic trauma accounting for approximately 8% of all trauma admissions.[58] Motor vehicle accidents account for the majority of these injuries (63–78%), with falls running a distant second (10–17%). Blunt chest wall injuries are more prevalent at extremes of age, disproportionately affecting adults >60 yrs of age, and children <12 yrs old. In children of <3 yrs of age, child abuse is the most frequent cause of thoracic injury.[59]

Distinguishing blunt chest trauma from other nonpenetrating injuries outside the head is the high mortality associated with it. Chest wall trauma is a strong indicator of severe internal injury, especially when rib fractures are present. In a study by Gaillard et al.[60] on trauma patients requiring admission to an intensive care unit, chest trauma increased the risk of death from 27% to 33%, with the precise rate varying with the extent of injury. Pneumothorax, hemothorax, pulmonary contusion, and flail chest were associated with risks of death of 38%, 42%, 56%,

and 69%, respectively. In another study by Ziegler and Agarwal[61] reporting on 7,147 patients seen by a trauma service, 711 (10%) had rib fractures, with 12% ($n = 84$) of these people ultimately dying. In chest trauma patients surviving the initial event, the most common cause of mortality is pulmonary complications. Severe thoracic injuries generally result in reduced vital capacity and forced expiratory volume, atelectasis, hypoxia, and hypercapnia and an increased prevalence of pulmonary infection.

To reduce morbidity and mortality, adequate pain relief is essential in chest trauma patients. Thoracic epidurals using LAs, opioids, or combinations of the drugs have been demonstrated in numerous studies to provide pain relief, improvement in pulmonary function, and a reduction in respiratory complications.[62,63] The main drawback to using epidural LAs is an increased risk of hemodynamic instability. When highly lipid-soluble narcotics such as fentanyl are administered epidurally, systemic blood levels approach those following intramuscular injections, which can lead to respiratory depression.[64]

In patients who are not candidates for epidural blockade, interpleural analgesia has been advocated as an alternative analgesic technique. The main complication of interpleural analgesia is pneumothorax. Although the development of pneumothorax can have severe consequences in patients with blunt chest trauma, the prevalence of clinically significant pneumothorax is <5%.

The results of outcome studies for interpleural analgesia in chest trauma have been mixed at best. Although some studies have reported good results with interpleural LA infusions,[65,66] others have failed to demonstrate any benefit when compared with placebo[67] or intravenous morphine.[68] Presently, interpleural analgesia remains a second-line treatment in blunt thoracic trauma.

Intercostal nerve blocks are another form of analgesia that can be used to treat somatic chest pain. A review of the literature revealed only one open-label study evaluating intercostal nerve blocks in patients with rib fractures.[69] Although respiratory function, as evaluated with a flowmeter, was found to significantly improve 1 hr after the nerve blocks, this effect had completely subsided 6 hrs after intercostal nerve blocks. Problems with intercostal nerve blocks include the risk of pneumothorax, high blood levels of LAs, lack of effect on visceral pain, the requirement for multiple levels to be blocked, and the short duration of action. However, in patients undergoing thoracotomy, cryoanalgesia of these nerves can provide significant, long-term pain relief.[70,71] For patients who require pharmacologic management of trauma-related thoracic pain, NSAIDS with opioids administered through a PCA device can provide effective analgesia.

Burn Injuries

There are very few things in life more devastating than a major burn injury. In the United States, >2 million burn injuries occur annually, with virtually all major ones requiring prolonged hospitalization, extensive rehabilitation, and psychological counseling. In addition to unremitting baseline pain, these patients must endure frequent dressing changes and wound debridements. In a study by Choiniere et al.,[72] the authors found that approximately half of all burn patients reported inadequate doses of pain medications for dressing changes. Moreover, a large subset of burn patients will go on to develop chronic pain.[73] Along with acute nociceptive pain and peripheral nerve damage, wind-up and central sensitization can occur, leading to secondary hyperalgesia. To improve outcomes and reduce the risk of developing chronic neuropathic pain, aggressive pain treatment is of the utmost importance in these individuals.

Topical Anesthetics. The application of topical antimicrobial agents is an essential element in preventing wound infection. Unfortunately, the use of some of these agents such as mafenide acetate (Sulfamylon) can be painful when applied to partial-thickness burn wounds. Silver sulfadiazine is a relatively painless topical wound agent that possesses broad antimicrobial effects. Some dressings such as Biobrane, a temporary semisynthetic skin substitute, and hydrocolloidal dressings may actually be associated with increased patient comfort.[74,75]

Although some researchers have reported topical LAs to be effective in treating burn pain,[11] other studies dispute this claim.[76] In patients with a compromised epidermis, the use of topical LAs can lead to systemic toxicity.[8,10] Intravenous lidocaine has also been described for pain relief in burn patients.[12]

Opioids. Opioids remain the mainstay of burn treatment worldwide.[77] Despite the increased metabolism and wide fluctuation of plasma proteins, the pharmacokinetics of intravenous opioids in burn patients does not differ significantly compared with patients without burns. Intramuscular or transdermal delivery of opioids is not suitable in patients with decreased tissue perfusion, as systemic absorption of drugs is poor.

The use of PCA opioids in burn patients is well established. The flexibility, rapid response to patients' fluctuating requirements, and elimination of the need for hospital staff to administer drugs makes PCA an ideal vehicle to deliver narcotic medications. In patients with background pain, we usually assess baseline opioid requirements and switch over to equi-analgesic doses of long-acting opioids, administering only breakthrough pain medications through PCA (i.e., no basal rate). Methadone is

unique among opioids in that it inhibits the reuptake of serotonin and norepinephrine, making it an effective treatment for neuropathic pain, and possesses antagonistic effects at the NMDA receptor.[78]

Procedural pain related to dressing changes and debridement represents a distinct challenge for physicians. Administering analgesics whose duration of action exceeds that of the procedure frequently leads to untoward side effects. For procedural pain, ultra–short-acting opioids such as alfentanil and remifentanil may be ideal choices. In one small, prospective, placebo-controlled study, the use of clonidine was found to reduce opioid requirements in patients with burn pain.[79]

Nonopioid Adjuvants. NSAIDS can used to treat burn pain, but their use in some patients may be associated with deteriorating renal function. In these instances, acetaminophen may provide an acceptable alternative. In a retrospective study evaluating pain management in 395 burned children, Meyer et al.[80] found that in 50% of patients, acetaminophen alone was sufficient to manage background pain.

Ketamine is an atypical anesthetic whose main use in medicine is as an anesthetic induction agent. In recent years, its amnestic properties, profound analgesic effects, and ability to preserve both respiratory and hemodynamic function have made it a popular drug for use in wound debridements and dressing changes. Although its untoward effects limit its use for background pain, in both oral and parenteral form, ketamine is ideally suited for procedural pain in burn patients unresponsive to opioids.[81,82]

Distinguishing pain from nociception is that, whereas the latter is a purely physiologic phenomenon, cognitive and emotional factors play a significant role in the pain experience. This may be especially relevant in burn patients, who often experience abnormally high levels of fear and anxiety. In these individuals, the use of sedative drugs such as benzodiazepines[23,83] or major tranquilizers like haloperidol[84] can provide beneficial effects.

Antihistamines are frequently used in burn centers for the management of anxiety, pain, and pruritus. The sensation of "itch," transmitted by polymodal C fibers, is sometimes worse than pain itself, especially during the healing phase of burn injuries. The sedative properties of antihistamines also make them useful in promoting sleep and relieving anxiety. Antihistamines may possess independent antinociceptive effects, and they have been shown to potentiate opioid analgesia.[85]

Regional and General Anesthesia. The limitations on regional anesthesia techniques make them inappropriate for a large percentage of burn patients. Even in patients for whom there are no contraindications to regional anesthesia, the burn and donor sites may extend beyond the area that can be covered with a single nerve block, sharply curtailing their utility. Nevertheless, the use of continuous epidural techniques, nerve blocks, and subcutaneous infiltration of LAs have all been described in burn patients.[86–88]

For burns limited to a limb, nerve blocks can be an effective method of pain control. With some of these procedures, the insertion of a catheter, enabling the use of continuous LA infusions, can be an especially attractive management option. In patients with severe pain uncontrolled with other modalities, general anesthesia is sometimes needed for wound debridements and dressing changes.[89,90]

Nonpharmacologic Treatments. In both the acute and chronic phases of treatment, burn patients may benefit from psychological counseling and social support systems. Fear, anxiety, depression, and nightmares are commonly seen in burn survivors. Not infrequently, posttraumatic stress disorder develops in the aftermath of a major burn. In these patients, counseling can be an indispensable addition to pharmacologic therapy in minimizing long-term psychological sequelae.

Hypnosis, biofeedback, and acupuncture have all been reported to reduce burn pain, but the lack of randomized, controlled trials limits the conclusions that can be drawn regarding these treatments.[91–93] Other relaxation techniques advocated for use in burn pain include visual imagery, therapeutic touch, and massage therapy.

Phantom and Stump Pain

According to the National Center for Health Statistics, there are >1.5 million amputees living in the United States.[94] Over a 9-yr period from 1988 to 1996, an average of 133,000 limb amputations were performed each year.[95] Although the large majority (82%) of these surgeries were for vascular conditions, trauma-related amputations comprised >16% of amputations, making it the second most common cause of limb loss. Approximately 97% of amputations are performed on lower limbs, with >70% of these being done below the level of the knee. Men are almost five times more likely to undergo a trauma-related amputation than women, with the risk of traumatic amputation in both sexes increasing steadily with age. In the upper limbs, trauma is the leading cause of acquired amputation (approximately 75%), with the highest rate being in men aged 15–45 yrs.[95,96]

The management of amputation-related pain is of paramount importance in the acute and chronic settings. Virtually all amputees experience "stump" (i.e., postoperative) pain immediately after surgery. This is expected after a major operation and is best managed with epi-

dural or regional anesthesia, if a catheter is present, or intravenous PCA. In contrast, pain that persists longer than the expected healing time may indicate a problem with the amputation. Although the reported prevalence varies widely, the prevalence of persistent stump pain is generally between 5% and 22%.[97,98] Although some authors report associations between pre-amputation pain, stump pain, and phantom pain, these relationships remain controversial.

There are two main categories of stump pain: that caused by injury to peripheral nerves and neuroplasticity and that caused by local pathology. Some of the recognized causes of stump pain include ischemia, surgical trauma, inflammation, skin infection, osteomyelitis, bone spurs, scar tissue, referred pain, neuromata, and ill-fitting prosthesis. The latter is perhaps the most common cause of stump pain and, if not corrected, can lead to skin ulcers and infection.[99] Whenever possible, the treatment of stump pain should focus on eradicating the underlying cause. Depending on the cause, this may include surgical revision, revascularization, antibiotics, or the injection of neuromas with LA and steroid.

The reported prevalence of phantom pain varies widely in the literature, ranging from <5% to almost 90%.[100,101] However, most recent studies report a prevalence of between 60% and 80%.[98,102] Several factors are known to influence the prevalence of phantom limb pain. Some studies have found phantom pain to be more likely to occur in upper limb amputations, proximal amputations (i.e., above the elbow or knee), and with amputations performed on the dominant arm.[103] Some,[104,105] but not all studies,[100,101] have found pre-amputation pain to predispose patients to phantom pain. Phantom pain is rare in cases of congenital absence and early childhood amputation, becoming more commonplace with age.[103] Most patients who experience phantom pain develop it within the first few days of amputation, although in rare cases it can take years to occur.[98,106] Characteristically, phantom sensations tend to abate over time, with the proximal portion of the limb disappearing first (telescoping). Phantom pain is believed to result from a combination of deafferentation, peripheral mechanisms, and CNS neuroplasticity.

In light of the high prevalence of phantom pain and the even greater prevalence of phantom sensations, a great deal of clinical research has been aimed at the prevention of these phenomena. In 1988, Bach et al.[107] carried out a controlled study in which 25 patients scheduled to undergo lower limb amputation were randomly assigned to receive either epidural blockade with bupivacaine and morphine 3 days before surgery or a control group that received conventional analgesics. Six months after the amputation, all 11 patients in the epidural group were pain free, whereas 5 of 14 patients in the control group experienced phantom pain. This important finding has been confirmed by some[108,109] but not all subsequent studies.[110,111] Of note, in the studies showing a preemptive effect for epidural analgesia, the infusions were started at least 24 hrs before surgical incision. The evidence to support the use of preemptive perineural analgesia to prevent postamputation is even weaker than that for epidurals.[112,113] However, considering the large percentage of patients with significant pre-amputation pain, the well documented benefits of surgical and postoperative epidural anesthesia, and the low risk involved, the authors believe preoperative epidural analgesia (or continuous nerve blocks for upper limb amputations and for patients who are poor candidates for neuraxial anesthesia) should be strongly considered for all scheduled amputations.

One indicator of the effectiveness of treatment for a disorder is the range of therapies advocated. For phantom pain, this number is exceedingly large, which is a telltale sign of the absence of any reliable, standardized treatment. The most studied anticonvulsant in the treatment of phantom pain is carbamazepine, which has been shown in several uncontrolled studies to be effective.[114,115] Recently, a double-blind, placebo-controlled, crossover study found gabapentin to significantly reduced phantom limb pain.[116]

Although TCAs have been shown to relieve neuropathic pain in a variety of conditions, only one controlled trial has evaluated their use in phantom pain. In this study, clomipramine and nortriptyline were found to be more effective than placebo in 24 patients with central pain, of which more than half had limb amputations.[117] In a double-blind, placebo-controlled, crossover trial comparing intravenous lidocaine and morphine in postamputation pain, whereas morphine reduced both stump and phantom pain, lidocaine was effective only for stump pain.[118] These results are consistent with a double-blind, crossover study by Huse et al.,[119] who found sustained-release morphine to reduce phantom pain and cortical reorganization. They are in contrast with an open-label study reporting the oral lidocaine analog mexiletine to be effective alone and in combination with clonidine in 31 patients with phantom limb pain.[120]

Several small, placebo-controlled studies have reported the NMDA receptor antagonists ketamine and dextromethorphan to be effective treatment for stump and phantom pain.[121–123] Two other drugs that have been shown to be effective in double-blind clinical trials are calcitonin and tizanidine.[124,125] Therapies that have been reported to be effective for stump and phantom pain in uncontrolled trials include beta blockers, TENS, motor cortex and spinal cord stimulation, dorsal root entry zone lesions, acupuncture, and intrathecal narcotics.[103,126,127]

Vertebral Fractures

In clinical practice, only 30% of vertebral fractures come to the attention of physicians, primarily because the lack of severe back pain in many patients does not trigger obtaining radiologic studies.[128] However, vertebral fractures are the most common type of osteoporotic fractures. The prevalence of radiographically demonstrated vertebral deformities increases from 5% in individuals between the ages of 50 and 54 yrs to 50% in women of >80 yrs of age.[129] The most common locations for vertebral fractures are at the thoracolumbar junction, the midthoracic spine (T7-8), and the lumbar vertebral column. Single vertebral body fractures are by far the most common type, followed by multiple contiguous fractures. The prevalence of spinal fractures is highest in white women, owing to their increased prevalence of osteoporosis.[130]

Spinal fractures represent a significant cause of morbidity and mortality in the elderly and thus demand prompt recognition and aggressive treatment (Table 4). The prevalence of neurologic deficits depends on the extent, type, and location of injury, but it is usually cited as being >30%.[131–133] Whereas a crushed vertebral body can cause sudden, severe compression of nerve roots as they exit the intervertebral foramina, vertebral fractures seldom result in spinal cord injury. The main goals of therapy in patients with spine trauma are: preserving of life, optimizing neurological function, and providing a stable, painless vertebral column.

Exercise programs for elderly patients suffering from spinal fractures have been shown to increase bone mineral density, decrease the use of analgesics, and improve quality of life.[134,135] Because patients with vertebral fractures are at increased risk to develop hip and other fractures, walking programs, fall-reduction courses, and even Tai Chi may be beneficial.[136,137]

NSAIDS remain the first-line pharmacologic treatment for bone pain, although in our experience, most patients who present with multiple spinal fractures require stronger analgesics. A good treatment plan is to begin with short-acting opioids, either via PCA or through oral administration, to assess opioid requirements. More than half of all patients with severe vertebral fractures will go on to develop chronic pain.[138,139] In these patients, we generally switch them to a long-acting opioid if their pain is continuous, with liberal doses of short-acting opioids on an as-needed basis to treat breakthrough pain. Advantages of sustained-release opioids include steady-state analgesic levels, lower cumulative doses, and the slower development of tolerance. When neuropathic (i.e., radicular) pain is present, an adjuvant medication such as an antiseizure drug or TCA can be beneficial.

In elderly patients with spinal fractures, equal emphasis must be placed on the prevention of future fractures. Two classes of drugs that have been shown in clinical trials to reduce the prevalence of vertebral fractures are bisphosphonates and salmon calcitonin, both of which act to inhibit osteoclastic bone resorption.[140,141] Calcitonin can be administered subcutaneously or intranasally, usually on a once-per-day or every-other-day dosing regimen. Both oral and parenteral forms of bisphosphonates are available, and depending on the medication, dosing can be daily, weekly, or even monthly. In addition to preventing fractures and improving outcomes, both of these drugs have been shown to be analgesic.[142,143]

In part, the high prevalence of chronic pain after spinal fractures may be due to altered spinal configuration. This finding has led to the development of interventions aimed at reducing anatomic defects. Percutaneous kyphoplasty entails inflating a bone tamp within the vertebral body to re-expand the fracture before injecting cement. Vertebroplasty involves the injection of an acrylic polymer into a partially collapsed vertebra. The best candidates for these procedures are patients with localized, axial back pain with evidence of a new or progressive vertebral compression fracture. Although success rates exceeding 67% have routinely been reported with these procedures, there have been no controlled studies to date.[144–147]

Spinal Cord Injury

Although vertebral fractures and spinal cord injury (SCI) sometimes go hand in hand, because the management is so different, they are considered separately. Less than a century ago, SCI was considered to be almost uniformly fatal. But dramatic advances in therapy have enabled thousands of individuals with SCI to live productive and fulfilling lives. Each year in the United States, approximately 100,000 persons sustain and survive SCI, with the large majority of these individuals being between 15 and 35 yrs of age. In descending order, the most common causes of SCI are motor vehicle accidents, falls, and sports injuries. Among the >200,000 individuals living in the United States with SCI, the reported prevalence of pain ranges from 18% to 77%.[148–151]

There are several different types of pain experienced by SCI patients. Mechanical and musculoskeletal pain can occur secondary to soft-tissue or bony injuries sustained after trauma, spinal fracture or instability, surgery, or muscle spasm or spasticity. Many pharmacologic and nonpharmacologic treatments have been advocated for spasticity, including potassium channel blockers, antiseizure drugs, botulinum toxin, skeletal muscle relaxants, dantrolene, serotonergic antagonists, benzodiazepines, gamma

TABLE 4
Clinical sequelae of vertebral fracture

Symptoms	Signs	Functions	Future Risks
Back pain	Height loss	Impaired activities of daily living	Increased risk of future fractures
Radiculitis	Kyphosis	Difficulty fitting in clothes due to kyphosis and protuberant abdomen	Increased morbidity and mortality
Anxiety	Decreased lumbar lordosis	Difficulty bending, lifting, and ambulating	
Depression	Protuberant abdomen	Frequent falls	
Fear of falling	Reduced pulmonary function	Pulmonary dysfunction	
Reduced quality of life	Weight loss		
Early satiety Insomnia	Weakness		

Adapted.[130]

aminobutyric acid B agonists, neurolytic blocks with alcohol and phenol, neuroablative surgical procedures, dorsal root entry zone lesions, TENS, neuromuscular stimulation, alpha-2 agonists, phenothiazines, and tetrahydrocannabinol.[152–158] However, a recent Cochrane database review focusing on SCI-related spasticity found strong evidence to support the use of only two agents, intrathecal baclofen and, possibly, tizanidine.[158] Table 5 provides a list of drugs that have been shown in clinical trials to be effective for spasticity related to SCI. For trauma and axial spine pain, NSAIDS, opioids, and the application of physical agents can be beneficial.

Central (dysesthetic) pain (CP) is the most common form of pain after SCI, with a prevalence exceeding 50%.[159] One of the hallmarks of CP is its incredible variability. Whereas the most common descriptors are adjectives such as burning, lancinating, and aching, some patients describe their pain as throbbing, pulling, or icy. Most cases of CP develop within weeks of injury. However, some patients report the onset to be immediate, and in others, the interval between injury and pain may exceed a year. CP usually occurs diffusely below the level of injury, although not uncommonly, it is localized to the transition zone. Allodynia is common, but not universal.[159–161] Patients with SCI sometimes go on to develop syringomyelia, a condition involving cavitation of the spinal cord. Although rare, syringomyelia is believed to have the highest prevalence of CP of any disease.[161]

There are many different theories about how CP develops and why only some patients experience it, but at present, the cause is unknown. Injury to spinothalamocortical pathways seems to be a necessary, but not a sufficient factor in the pathogenesis of CP. Studies have implicated a wide range of possible mechanisms such as sympathetic dysfunction, release of normal inhibitory control by CNS lesions, and several different binding sites, including the NMDA receptor and sodium channels, as being responsible for CP.[159]

In light of its resistance to conventional therapies, CP is one of the most challenging conditions physicians confront. There are several controlled trials evaluating antiseizure medications in SCI. Gabapentin has been shown to be beneficial in reducing some forms of neuropathic pain after SCI, and may be more effective when given within 6 mo of the onset.[162,163] In another randomized, placebo-controlled trial assessing lamotrigine in SCI central pain, although no statistically significant effect was noted on the total sample, in patients with incomplete SCI, the treatment group was found to have less spontaneous and evoked pain.[164]

In a double-blind study by Attal et al.,[165] intravenous lidocaine was found to significantly (≥50%) reduce spontaneous pain and tactile allodynia in 10 of 16 patients with CP, a majority of whom suffered SCI. Interestingly, in another placebo-controlled study assessing the effect of the oral analog mexiletine in SCI dysesthetic pain, no benefit was found.[166] Possible reasons for this discrepancy include the relatively low dose of mexiletine administered (450 mg/day) and a differential effect on sodium channels and other receptors.[167,168]

In studies of other classes of medications, the NMDA receptor antagonist ketamine has been shown in two controlled trials to be effective

TABLE 5
Medications shown in clinical trials to be effective treatments for spinal cord injury—related spasticity

4-Aminopyridine
Cyproheptadine
Clonidine (oral, intrathecal, and transdermal)
Baclofen (intrathecal and oral)
L-threonine
Gabapentin
Orphenadrine
Dantrolene
Botulinum toxin (injections)
Tetrahydrocannabinol (oral)

for CP caused by SCI.[169,170] The TCA amitriptyline and trazodone, two drugs that preferentially inhibit the reuptake of serotonin, were not found to be effective in SCI pain.[171,172] This is in contrast to another randomized, controlled study that found amitriptyline to be effective in CP after stroke.[173] This discrepancy may reflect different underlying pain mechanisms for the two disorders.

Opioids have been studied in SCI, and they have been found to reduce at least some of the components of central neuropathic pain.[169,174] In one double-blind study assessing the efficacy of intrathecal morphine and clonidine in pain after SCI, the combination of the two drugs was found to be superior than either drug by itself.[175] In spinal cord–injured patients with refractory pain, other therapies that should be considered include 4-aminopyridine infusions, transcranial electrical stimulation, intrathecal baclofen, microsurgical dorsal root entry zone lesions, and motor cortex stimulation.[154,176–179]

Although CP and spasticity- or spasm-related pain are the most common types of pain in SCI, they are not the only sources of patient discomfort. Pressure ulcers are frequently encountered in paraplegics, with one study finding a 55% prevalence in patients admitted to a spinal injury unit.[180] The proper treatment of pressure ulcers must encompass several different goals, including the acceleration of wound healing, relief of pressure and prevention of future ulcers, surgical or chemical debridement, and pain management. NSAIDS may be helpful as adjuvants but are often insufficient by themselves. Because pressure ulcers often result in constant pain that lasts for months, sustained-release opioids may be necessary. There are no clinical trials evaluating neuropathic medications in decubitus ulcers. However, because chronic, unrelenting pain can lead to central sensitization and wind-up, in patients who describe their pain as burning, shooting, or lancinating, a trial with neuropathic medications may be worthwhile.

The prevalence of visceral pain, or deep, diffuse pain in the pelvis, abdomen, or thorax, has been reported in previous studies as ranging from 0% to 28% after SCI.[181–183] Although no clinical trials have been done to assess the role of pharmacotherapy in SCI visceral pain, literature exists to support the use of TCAs in functional chest pain and gastrointestinal disorders.[184,185] In refractory visceral pain unresponsive to other therapeutic modalities, opioid therapy should be instituted. Other types of pain that may be encountered when treating SCI patients include shoulder pain from wheelchair use, long-bone fractures from disuse osteoporosis, deep-vein thrombosis, and radicular pain. The latter can be treated with epidural steroid injections or neuropathic pain medications.

Traumatic Brain Injury

Traumatic brain injury (TBI) is another common cause of pain and disability, affecting nearly 5 million people in the United States. Of the nearly 1.5 million Americans sustaining TBI each year, the number of patients who go on to experience long-term disability is estimated to approach 80,000–90,000 annually. Young adults between the ages of 18 and 25 and the male sex of all ages are at highest risk to suffer TBI, with smaller peaks in prevalence occurring in the geriatric and pediatric age groups. Among TBI cases, the majority are secondary to motor vehicle accidents, followed by violence and falls. The prevalence of pain in patients who experience TBI ranges from 18% to 95%.[186–190]

The prevalence of pain, both acute and chronic, is largely dependent on the severity of TBI. Mild TBI has traditionally been defined as cases with an initial Glascow Coma Scale score of 13–15, with a loss of consciousness of <1 hr. TBI is classified as moderate or severe when the Glascow Coma Scale score is ≤12, or loss of consciousness exceeds 1 hr. Regardless of the classification, the most frequently encountered pain complaints in TBI are headache, musculoskeletal pain, spasticity, neuropathic pain, and facial pain.[187–193] Table 6 contains the approximate percentage of patients reporting chronic pain broken down by site and the extent of injury.

Headache is the most common pain complaint in patients with TBI, with mild TBI patients reporting a greater prevalence than those with more severe disease.[187–189,194] In one study, the prevalence was noted to be 89%.[188] Unfortunately, there is scant literature to support the use of any one class of analgesics in the treatment of TBI-associated headache. In an open-label study assessing the use of the monoamine oxidase type A inhibitor moclobemide in 26 TBI patients with major depression, the authors reported a 39% decrease in pain scores and marked (>80%) reductions in both depression and anxiety.[195] However, pain complaints in this study were not limited to just headache. In the reports evaluating the TCA amitriptyline, one of the most commonly utilized medications in migraine and tension-type headaches, the outcomes have been mixed.[196–198] In a double-blind, placebo-controlled study evaluating the gamma aminobutyric acid derivative Piracetam in postconcussion syndrome, the drug was found to significantly reduce the occurrence of headache and several other bothersome symptoms.[199] Other classes of medications that should be considered in treating TBI-related headache include NSAIDS, antiepileptics, selective serotonin reuptake inhibitors, beta-blockers, calcium-channel blockers, and steroids.

In patients with mild TBI and

TABLE 6
Proportion of patients with traumatic brain injury (TBI) reporting chronic pain by location

	Mild TBI, %	Moderate/Severe TBI, %
Head	69	28
Neck/Shoulders	40	16
Back	32	11
Limbs[a]	21	23

Data were extracted from Lahz and Bryant[187] and Uomoto and Esselman.[188]
[a]Represents an approximation.

head injuries not accompanied by loss of consciousness, persistent neck pain and occipital headaches can be a major source of disability.[189] This injury pattern is particularly common after rear-end motor vehicle accidents. For patients with posttraumatic cervicogenic headaches or cervicalgia, radiofrequency denervation of the medial branches innervating the cervical facet joints may provide long-term pain relief.[200,201] Other sources of whiplash injuries include cervical disc disease, myofascial pain, ligamentous damage, and neuralgias.

With moderate to severe TBI, the development of spasticity can contribute to chronic pain. Typically seen as extensor hypertonia most prominent in the lower limbs, the management of spasticity in these patients is of paramount importance. Pharmacologic agents, which can be administered by a variety of different routes, play a critical role in the management of upper motor neuron syndromes. There are numerous studies evaluating continuous intrathecal baclofen infusions in TBI patients that demonstrate a beneficial effect on pain and spasticity,[202–204] including one in children.[205] In patients with regional spasticity, injections of botulinum toxin or alcohol neurolysis have been shown to produce good outcomes.[206–208] Disadvantages of these two techniques include the need to repeat the procedure when the effects dissipate. In addition, neurolytic blocks frequently result in the formation of painful neuromas after nerve regeneration. Other treatments that might be beneficial in TBI-induced spasticity include the alpha-2 agonist tizanidine, cutaneous electrical stimulation, and cryotherapy.[208–211]

CONCLUSIONS

The management of pain plays a critical part in the treatment of trauma patients. Trauma exerts pervasive effects on a multitude of body systems, many of which contribute to morbidity and mortality. These effects involve not only physiologic responses, but psychological ones as well. In recent years as physicians have come to better understand the mechanisms and consequences of pain, it has become increasingly clear that the prompt and proper treatment of pain can actually improve outcomes. Because of the capricious nature of trauma pain, regular assessment of patients and frequent adjustments in medications, dosages, and techniques are necessary. More research is needed to better elucidate the role pain plays in the body's response to trauma and to help clinicians find better ways to treat it.

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Mission Statement

The mission of the *American Journal of Physical Medicine & Rehabilitation* is to publish articles about all aspects of PM&R and to promote excellence in education, scientific research, clinical practice, health policy, and administration.