AMPUTATION AND PHANTOM LIMB PAIN: A PAIN-PREVENTION MODEL

Introduction

Pain as part of human existence has been depicted from the time of the earliest cave paintings, long before the beginning of written history. Bone decalcification and tubercular lesions are described on skeletons from 7,000 years ago. Cave art and sculpture depict childbirth, injury, and death, all undoubtedly associated with pain. Our earliest written and oral history also communicates pain from injury and death from battle with beasts and humankind. Pain takes many forms, and one of the more interesting forms of pain is explored in this article: phantom limb pain. First described by Pare, a French surgeon in 1551, this form of pain was so named because it refers to a patient’s descriptions of pain in places that no longer exist: amputated limbs.

The history of our field’s evolving recognition of pain, and specifically pain associated with amputation is associated with Larrey, Napoleon’s surgeon general, who recorded in his 1807 memoirs that extremely cold weather (as cold as –19°F) allowed him to perform painless amputations on the battlefield. Mitchell was later thought to be the first to use the term “phantom limb pain” when he published a long-term study of the fate of civil war soldiers, and Melville accurately described Captain Ahab’s phantom limb in Moby Dick. Amputation and the resulting problems were described widely in the history of military medicine among adults; however, all age categories are represented in illness and injury. Unfortunately, at one point in early 20th century a paper stated that young children did not experience real pain. Fortunately, the topic has been restudied, and more sophisticated analysis has confirmed that children indeed experience pain in general and phantom pain specifically.

There are approximately 203,000 surgical amputations performed in the United States each year (Janice McDonnell, personal communication, Amputee Coalition of America, 1999). Studies show that as many as 70% of amputees suffer burning, cramping, and other qualities of phantom pain during the first few weeks after amputation. Non-painful phantom sensations, or rather the patient’s observation of occasionally feeling the presence of the missing part, are almost universal. More problematic, even 7 years after amputation, 50% still continue to have burning, cramping, throbbing, or crushing phantom limb pain, described as continuous or intermittent. Some patients describe the pain as crushing, twisting, like being stabbed with needles, or that the phantom limb is malpositioned. There is some evidence that preamputation pain increases the risk of phantom limb pain, in fact, phantom limb pain may be a manifestation of preamputation pain. This could explain why diabetics have less phantom limb pain, and the same is true for paraplegics who undergo amputation.

It is possible to focus on this single novel and interesting model of pain and fail to fully appreciate that the presence of phantom limb pain does not insulate amputee patients from pain caused by other factors such as trauma and preexisting injuries. Moreover, amputation can indirectly cause other forms of pain; coexisting musculoskeletal pain occurs as people with injuries or surgical amputations attempt to ambulate and perform other daily activities while guarding injured.
anatomy. As the amputee patients adapt, they begin to do lifting, maneuvering, and weight bearing with body parts not designed for those functions. They use nonconventional postures and gaits and use joints and muscles outside of normal design limits. Overuse pain syndromes lead to compensatory musculoskeletal use, causing strain, injury, inflammation, and further pain.

There is a positive correlation between having a painful limb before amputation and the likelihood of phantom limb pain after surgical amputation. Studies of this problem demonstrated that the use of preemptive epidural analgesia on painful limbs for 3 days before surgical amputation decreased the incidence and severity of phantom limb pain after surgery.

Before we can explore management, the CRNA needs to be aware of pain subtypes. Raj categorizes pain by:

1. Acute pain (somatic and visceral)
2. Postoperative pain
3. Neuropathic pain
4. Terminal pain (eg, cancer pain)
5. Chronic pain
6. Psychogenic pain

Phantom limb pain is an example of chronic nonmalignant pain and frequently, or more specifically, neuropathic pain. Although commonly described after limb amputation, it also has been described after the loss of teeth, fingers, intestines, breasts, and the penis.

Phantom pain can have lifelong effects on amputee patients and their families. The economic toll for chronic nonmalignant pain in the United States is more than $100 billion per year. When considered collectively, these patients make a substantial impact on national healthcare economics.

A growing number of reports suggest that we can make a substantial difference in alleviating this form of human suffering. Authors are beginning to use the term prevention. The goal of this article is to provide information on the mechanisms involved in phantom limb pain, interventions, and the potential for prevention. Certified Registered Nurse Anesthetist (CRNA) pain managers can focus technical skills and team facilitation on treatment and potential prevention of phantom limb pain and this form of lifelong suffering.

The pain process

Bach reiterated the International Society for the Study of Pain's definition of pain, “as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” Other elements of this pain problem include inflammatory and neuropathic pain. The former refers to pain associated with peripheral tissue damage, eg, that produced during surgery, and the latter refers to pain caused by damage to the nervous system. Nociception is the process in which stimuli ascend the nociceptive pathways from the periphery to the central nervous system (CNS). The term “pain” is applied after those stimuli have been processed in neuromatrix and integrated with memory into perceptions and awareness. In the case of phantom limb pain, overall CNS stimulation causes nociceptive neuron changes much like an electrical circuit carrying an excessive current load with resultant burnout. Bach describes 4 subprocesses in the overall mechanism pain causation:

1. Transduction: noxious stimuli lead to electrical activity in primary afferent fibers at the tissue level.
2. Transmission: noxious stimuli are conveyed to second order neurons in the spinal cord and to the somatosensory cortex.
3. Perception: noxious stimuli are translated into sensation.
4. Modulation: the nervous system returns information to the spinal cord neurons affecting the flow in incoming nociception.

These 4 processes indicate possible sites for pain management intervention.

Mechanisms of pain: The periphery

At the site of injury, a variety of tissue release factors begin the nociceptive process. Cousins and Bridenbaugh refer to these factors collectively as the “sensitizing soup,” chemicals that result from tissue injury causing pain and inflammation. A partial list of the contents of this soup includes potassium, prostaglandin, substance P, leukotrienes, histamine, serotonin, and norepinephrine. This chemical soup, along with local acidosis and microcirculatory ischemia, initiates changes in the sensitivity of primary nociceptors, resulting in a decreased threshold for subsequent nociceptive depolarization. Evidence suggests that prolonged nociceptive stimulus can bring into play a group of super high-threshold nociceptors, otherwise silent, that become active only after high-intensity, prolonged noxious input such as from amputation.

At the periphery, effective analgesics for the control of postamputation pain include nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetics, and nonpharmacologic measures, such as heat and cold. Proper stump-wrapping also is important, as it promotes venous return, aiding in the reintegration of microcirculation disruption responsible for what patients describe postoperatively as “throbbing pain.”

Mechanisms of pain: The nerves

The terminals of nociceptors and their microenvir-
ment have been described as “a jungle through which a scientist has difficulty in forging a route to find the secrets contained within.” More simply, Cousins and Bridenbaugh state that once the peripheral nociceptors have been activated, the sensory impulses travel toward the CNS by either myelinated or unmyelinated primary afferent neurons.

These primary afferent neurons are classified into 3 major groups based on the size of the axon, the degree of myelination and conduction velocity: groups A, B, and C, respectively. Group A is further subdivided into subgroups alpha, beta, gamma, and delta. Under normal circumstances, the small diameter (<3 µm) and relatively fast conducting myelinated A-delta fibers carry the initial nociception. The small (<1 µm) and slow unmyelinated C fibers carry the prolonged nociceptive impulses, which continue long after the injury has taken place. Large diameter (8 µm) and faster conducting myelinated A-beta fibers carry innocuous impulses such as touch and pressure. The largest diameter (15 µm) fibers conduct motor function.

Mechanisms of pain: The cord
Nociceptive impulses enter the cord via the dorsal horn where they synapse with second-order neurons. It is here that incoming nociception is affected by modulation from higher centers. In other words, the brain has the ability to “adjust the volume” of incoming pain signals and offers clues to intervention.

Nociceptive impulses pass directly to the anterior horn of the cord and stimulate sympathetic neurons to produce reflex responses, for example, the release of norepinephrine affecting sympathetic outflow to the affected part. The stimulus also crosses to the contralateral side of the cord, passing cephalad to the brain stem and provoking pain behaviors such as flinching and reflexive withdrawal from the perceived stimulus. With more cephalad spread of the stimulus comes integration of memory and emotional processes. This is when the stimulus is interpreted as pain. Resulting responses can include the classic “fight or flight” response, immobilization, and vocalizations such as crying. This process triggers memory formation of the unpleasant experience. Organisms attempt to avoid repetition of the experience.

Neuroplasticity and “wind up”
Evidence has added insight into the CNS, including its capacity for plasticity and adaptation. Prolonged stimulus can induce a hyperexcitable state called “wind up,” which may lead to the establishment of pain memory. Plasticity, or the ability of the CNS to change its synaptic connections in response to changing conditions, can result from sensitization of neurons in the dorsal horn. This central sensitization is manifested as an increased response to afferent input, an expansion of the receptive fields of peripheral nerves, and an increase in spontaneous activity.

After the CNS is stimulated by the alarm signal of nociception and pain, it can become “more sensitive” to painful stimuli, that is, lower the threshold level that existed in the pre-pain state. The sensory fields of the primary nociceptors expand in response to the stimulus. Thus, the patient may report what normally might be minor nociceptive transmissions as more painful, and the tissue around the wound can become more sensitive than would be considered normal. By definition, allodynia is pain arising from a stimulus that would not otherwise cause pain. Hyperalgesia is an increased response to a normally painful stimulus.

Contradictory findings lend credence to this model of the CNS as an organ capable of plasticity but also a hardwired system. As mentioned, pain before surgery is associated with an increased incidence of postoperative phantom limb pain. However, phantom limb pain in children with congenital limb absence due to thalidomide also has been reported. Phantom limb sensation is strongest in above-elbow amputation and weakest in below-the-knee amputation. The incidence of phantom limb pain increases with the age of the amputee. The neuroplasticity of the CNS can explain these seemingly contradictory findings.

Prolonged noxious input causes C fibers within the dorsal horn to release synaptic transmitters such as aspartate, substance P, and the excitatory neuropeptide, glutamate. These chemical factors begin a cascade of events that leads to long-term changes in neurocellular function. Under normal circumstances, the ion channel adjacent to the N-methyl-D-aspartate receptor is blocked. However, in the presence of aspartate and glutamate released by the nociception process, this ion channel becomes unblocked, allowing for influx of Ca+ and further depolarization of afferent nociceptive pathways. Interestingly, Salmon-Calcitonin has been shown to be effective in phantom limb pain. Substance P initiates a slow and prolonged depolarization of afferent nociceptive pathway which can sustain pain long after the initial tissue injury. Nerve injury–induced neuropeptides may increase the release of nerve growth proteins, triggering central sprouting of primary afferent neurons. This can cause an enlargement of the cut nerve ending or a neuroma. This neuroma is a concentration of sensory fibers, more dense than in the pre-injury tissue and capable of high sensitive and ectopic firing.

Clinical implications: Preoperative phase
Evidence has suggested that after tissue damage and in the presence of constant high-intensity bombard-
recently developed nonmechanical constant infusion devices, eg, the Ethicon ON-Q or Pain Buster (both from I-Flow Corporation, Lake Forest, Ill). These devices, about the size and shape of a racquetball, function in the reverse of the common “hand-grenade” wound suction. They are designed to instill local anesthetics at different flow rates and with different durations of infusion, eg, from 0.5 to 5.0 mL/h over 2 to 5 days. This single-use plastic device can supply local anesthetics directly to wound or nerve without cumbersome pumps that can limit early ambulation.

Epidural analgesia with an opiate/local anesthetic combination is safe, efficacious, and widely accepted for severe postoperative pain. In addition, epidural infusions are easily titrated to specific patient requirements. Psoas block or peripheral nerve blocks, such as the “3-in-1” femoral nerve block, can augment other forms of pain management modalities and provide an opportunity to limit high-dose narcotic adverse effects. Hopefully, intravenous patient-controlled analgesia would be available if neuroaxial anesthesia/analgesia were not. Since we know that Visual Analogue Scale pain scores will most likely be consistently high for the first several days, an intravenous patient-controlled analgesia regimen that includes a constant or basal dose in addition to the patient-controlled analgesia doses would be rational, along with inclusion of NSAIDs, cold, proper stump-wrapping, elevation, and early support team interventions.

Nonpharmacologic interventions Nonpharmacologic pain therapies also can be highly effective and have a high therapeutic ratio. For example, Tverskoy et al noted that patients receiving preincisional doses of ketamine (2 mg/kg) experienced decreased hyperalgesia following surgery. Physical therapy maximizes function by training amputated muscle groups and strengthening other muscles to compensate for missing structures, thus preventing secondary muscle and joint strain and injury. Physical therapy also aids in the reversal of the general deconditioning caused by prolonged inactivity secondary to trauma and surgery. Massage therapy aids in relieving the muscle spasms in affected parts and tension in muscle groups compensating for missing structures. Heat and cold are effective in aiding healing and analgesia.

Psychological consultation to address stresses experienced by amputees can be valuable before surgery; however, windows of opportunities for such consultation are frequently narrow. Prepared amputee volunteers and support groups offer general reassurance and advice about stump and prosthesis care and can be an ongoing source of support and adjustment for the amputee and life-partners. For example, amputee community resources offer aid with less frequently addressed issues, such as adaptation of living space and postamputation sexuality. Unfortunately,
these types of referrals are not thought of until the postoperative phase, if at all. Occupational therapists help amputee survivors maximize functioning and effectiveness, as well as regain self-confidence. Spiritual resources are useful for aiding the amputee in the journey from patient to survivor.15

Clinical interventions: Long term
CRNAs who work in pain management are the natural and logical resource for the management of chronic phantom limb pain. Almost all amputees have phantom sensations and occasionally phantom pains, both of which can range from just enough to enter conscious recognition to disturbingly painful. Simply telling them “it’s all in your head” does patients and our profession a disservice.

Findings on the psychological components of phantom limb pain are mixed. Bach4 refers to a study of people with chronic pain that shows that depressed patients are more likely to report greater pain intensity and exhibit more pain behaviors and interference with life activities, and these results agree with the general symptoms of depression in chronic pain states. However, anxiety symptoms were reported more often than depression among the amputees who reported phantom limb pain, and Bach4 stated “the prevalence of depression was low, suggesting that it is an uncommon reaction to amputation…. In addition, we found no relation between the experience of pain and emotional distress, suggesting that phantom pain is not a function of emotional adjustment.”

Antidepressants are helpful in many form of chronic pain. First, they are effective treatment for understandable depression after losing a part. Secondly, the tricyclic antidepressants, eg, amitriptyline and trazodone, demonstrate effectiveness in downward modulation of nociception. An effect likened to the body “turning down the volume” on incoming nociception. This effect has not been shown with benzodiazepines or selective serotonin reuptake inhibitors, such as paroxetine (Paxil) or fluoxetine (Prozac). In another category, membrane stabilizers, such as anticonvulsants, can inhibit irritable nociceptive foci and are considered first-line drugs for the treatment of chronic neuropathic pain. Gabapentin has become a popular and effective agent for the treatment of neuropathic pain. Although not favored for downward modulation, clonazepam and other benzodiazepines are effective for relief of lancinating phantom limb pain and muscle spasm.6 Ramamurthy7 has become a popular and effective agent for the treatment of chronic neuropathic pain. Gabapentin is useful in these types of referrals is not thought of until the postoperative phase, if at all. Occupational therapists help amputee survivors maximize functioning and effectiveness, as well as regain self-confidence. Spiritual resources are useful for aiding the amputee in the journey from patient to survivor.15

Clinical interventions: Long term
CRNAs who work in pain management are the natural and logical resource for the management of chronic phantom limb pain. Almost all amputees have phantom sensations and occasionally phantom pains, both of which can range from just enough to enter conscious recognition to disturbingly painful. Simply telling them “it’s all in your head” does patients and our profession a disservice.

Findings on the psychological components of phantom limb pain are mixed. Bach4 refers to a study of people with chronic pain that shows that depressed patients are more likely to report greater pain intensity and exhibit more pain behaviors and interference with life activities, and these results agree with the general symptoms of depression in chronic pain states. However, anxiety symptoms were reported more often than depression among the amputees who reported phantom limb pain, and Bach4 stated “the prevalence of depression was low, suggesting that it is an uncommon reaction to amputation…. In addition, we found no relation between the experience of pain and emotional distress, suggesting that phantom pain is not a function of emotional adjustment.”

Antidepressants are helpful in many form of chronic pain. First, they are effective treatment for understandable depression after losing a part. Secondly, the tricyclic antidepressants, eg, amitriptyline and trazodone, demonstrate effectiveness in downward modulation of nociception. An effect likened to the body “turning down the volume” on incoming nociception. This effect has not been shown with benzodiazepines or selective serotonin reuptake inhibitors, such as paroxetine (Paxil) or fluoxetine (Prozac). In another category, membrane stabilizers, such as anticonvulsants, can inhibit irritable nociceptive foci and are considered first-line drugs for the treatment of chronic neuropathic pain. Gabapentin has become a popular and effective agent for the treatment of neuropathic pain. Although not favored for downward modulation, clonazepam and other benzodiazepines are effective for relief of lancinating phantom limb pain and muscle spasm.6 Ramamurthy7 has become a popular and effective agent for the treatment of chronic neuropathic pain. Gabapentin is useful in
Figure. Certified Registered Nurse Anesthetist intervention in the prevention of phantom limb pain*

![Flowchart diagram of intervention strategies for phantom limb pain]

**Patient with phantom pain**

**A Successful ambulation with prosthesis**

1. **Pain goes away**
   - **B Burning**
     - Stump temperature and thermography show decreased blood flow to stump
     - Temperature biofeedback and relaxation to stump muscles daily for 2-wk maximum
     - If no relief, TENS† to stump, maximum of 3 trials per electrode-application area
     - If no relief, apply nitropaste to stump
     - If no relief, sympathetic blockade 3 x at 1-wk intervals
     - No relief

2. **Pain does not go away**
   - **C Cramping**
     - Muscle tension biofeedback and relaxation training daily x 2 wk
     - Home exercises
     - Add muscle relaxants (Valium 2 mg) for 4-wk maximum
     - No relief
     - TENS† trial x 3
     - Determine electrode location, unit type, and waveform characteristics by trial and error
     - No relief after 48 hr
   - **D Lightning**
     - Neurologic examination and EMG†
     - Exclude: neurologic lesion
     - Examine stump for neuroma
     - Inject with Marcaine/steroid solution and Use ultrasound after Injection or Phonophoresis daily x 14 days
     - Temporary pain relief obtained
     - Repeat injection 2 x at 48-hr intervals
     - Pain relief only temporary
     - Consider: Surgical excision

3. **F**
   - Tell patient no relief may be possible
   - Psychological testing (including MMPI†) to identify masked depression, situational anxiety, and hysterical reaction
   - Pain log for 1 wk-1 month to identify patterns and exacerbating events and times of day
   - Too much attention to pain may increase its importance in patient's life
   - Constantly evaluate prosthesis for lack of fit and alignment

---

* Reprinted with permission from Ramamurthy.15
† EMG indicates electromyogram; MMPI indicates Minnesota Multiphasic Personality Inventory; TENS indicates transcutaneous electrical nerve stimulation.
ing the more than 200,000 surgical amputations performed in the United States yearly and their subsequent chronic morbidity. Some studies and authors imply that preemptive analgesia in combination with effective, sustained multidisciplinary and multimodal pain management can actually limit or prevent phantom limb pain. It also is easy to argue that the prevention of a chronic pain problem could be more cost-effective than management of an established pain pattern. In the meantime, Raj¹ has written, “... because of the low success rate in treatment of chronic phantom limb pain, the prevention of pain by preoperative psychological and educational support and the provision of perioperative pain control cannot be overemphasized.” However, enticing the results, thus far, this topic needs further detailed study to refine our model of phantom limb pain, its treatment, and possible prevention.

REFERENCES

AUTHOR
Thom Bloomquist, CRNA, MS, FAAPM, has recently joined the Anesthesia/Pain Management Department at Cottage Hospital, Woodsville, NH. This article originated during the master’s degree completion program for practicing CRNAs and won the Graduate Writing Award at Rush University.

ACKNOWLEDGMENTS
I express my deep appreciation to several whose expertise was invaluable in the preparation of this article: Margaret Faut-Callahan, CRNA, DNSc, FAAN; James Godwin, MD; Ira Gunn, CRNA, MLN, FAAN; Vismal Kumar, MD; Virginia Maikler, RN, PhD; Janice McDonnell, the Amputee Coalition of America; Christina Skoski, MD; and Liz Zemke, RN.