This article defines the three major forms of postamputation sensation: 1) phantom sensation, 2) phantom pain, and 3) residual-limb pain. Proposed etiologies for phantom pain are discussed. The literature on current diagnoses and treatments for each of the three postamputation sensations is reviewed. (J Am Podiatr Med Assoc 91(1): 23-33, 2001)

Pain has been defined by the International Association for the Study of Pain as an “unpleasant sensory and emotional experience arising from actual or potential tissue damage, or described in terms of such damage.” The evaluation of pain in the amputee presents many problems unique to this population. This review will cover the different classifications of amputee pain and sensation, proposed etiologies of phantom pain, and current treatment options.

**Classification**

One of the difficulties in interpreting the literature on amputee-related pain is the previous lack of universal definitions for various sensations experienced by this patient population. However, it is now generally accepted that there are three main categories: 1) phantom sensation, the nonpainful feeling that the body part is still present; 2) phantom pain, a painful sensation perceived in the region of the missing body part; and 3) residual-limb pain, pain arising from the residual body part.

**Phantom Sensation**

The sensation of the presence of a missing limb following amputation was first described by Pare in 1551. The term “phantom limb” was first used by Mitchell in 1872. Phantom sensations include all nonpainful sensations perceived in the amputated limb. These may include fatigue, tickling, itching, wetness, cold, heat, pressure, and touch. Phantom sensation can also be kinesthetic and may include volume, position, and movement of the phantom limb. The sensations may vary in intensity and quality over time.

The incidence of phantom sensation was previously reported to be between 5% and 10%, but is now thought to be a nearly universal occurrence. Phantom sensation is often present immediately following the amputation surgery. It is more commonly found in the richly innervated distal aspect of the amputated extremity, such as the fingers or toes. Telescoping of the phantom limb may occur in up to 30% of patients. This phenomenon is described as a feeling that the distal parts of the limb are moving proximally.

Phantom sensation was previously thought to be absent in children with congenital amputations or limb deficiencies. However, recent reports suggest that this is not the case. The sensations experienced by congenital amputees do not appear to be as vivid as those experienced by acquired amputees.

**Phantom Pain**

Phantom pain is a painful sensation perceived in the region of the missing limb. The incidence is reportedly between 72% and 80% postoperatively and between 3% and 10% after several years. Proximal amputations have a higher incidence of phantom pain.
than distal amputations. Patients who experience preamputation pain are at increased risk for phantom pain, which may or may not resemble their preamputation pain. Pain is also more frequently experienced by patients who have a “telescoped phantom limb” that is perceived as short and fixed.\(^{14}\)

The following six physiologic variables have been linked with an increased incidence of phantom pain\(^{15}\): 1) a limb-threatening illness lasting for longer than 1 year prior to surgery; 2) multiple past surgeries; 3) acute osteomyelitis; 4) history of poor wound healing; 5) chronic pain in the limb prior to surgery; and 6) multiple past illnesses. Seven psychological factors are also consistently noted in individuals who develop phantom pain\(^{15}\): 1) lack of psychological support; 2) recurrent depression; 3) tendency to develop psychosomatic symptoms; 4) unusually rigid or compulsive behavior; 5) superstitiousness; 6) high degree of insecurity; and 7) body-image problems. The onset of pain generally occurs within the first week after amputation, but may not occur for several months or for years. The first 6 months often see a decline in the frequency, duration, and intensity of pain episodes. Pain persisting beyond 6 months is extremely difficult to treat and usually does not change in character after that time.\(^4\)

Phantom pain was originally thought to be psychologically based, and many patients were afraid to report it for fear of being considered mentally ill or of jeopardizing their relationship with their healthcare professionals.\(^7\) This myth has since been dispelled by several studies.\(^{16,17}\)

Phantom pain can vary widely in intensity, frequency, duration, and type. The pain may be shooting, shocking, cramping, stabbing, burning, characterized by the perception of unnatural positioning of the phantom limb, or squeezing.\(^{18}\) It is often reported as being knife-like or lancinating in the initial postamputation period and eventually progressing to take on a more squeezing, burning, or cramping quality.\(^{14}\)

The pain may be exacerbated under emotional stress; with exposure to cold or local irritants; during orgasm for a woman and after orgasm for a man; and during bladder catheterization, defecation, micturition, and smoking. Alleviating factors include early use of a prosthesis, massaging the residual limb, heat, and distraction.

It is possible that referred pain could mimic phantom pain, and this possibility should also be kept in the differential diagnosis. An example would be cardiac pain referred into the left upper extremity of a forequarter amputee. Treatment of the cause of the referred pain will relieve the pain.

### Residual-Limb Pain

Residual-limb pain arises from the residual limb rather than from the area of the missing body part.\(^4\) All amputees who are sensate will experience postoperative residual-limb pain. This type of residual-limb pain will improve quickly with healing of the incision site. Jensen et al\(^{19}\) reported that 57% of patients continued to have residual-limb pain at 8 days following amputation, 22% at 6 months, and only 10% at 2 years.

An excellent review by Davis\(^4\) noted six common causes of residual-limb pain. The pain may be prosthetic, neurogenic, arthrogenic, sympathogenic, referred, or related to abnormal residual-limb tissue.

**Prosthetic Pain.** This is the most common type of residual-limb pain and arises from an improperly fitting prosthesis. Causes to be considered during the evaluation of prosthetic pain are poor socket fit, inappropriate suspension, painful adductor roll in the above-the-knee amputee, distal residual-limb weightbearing, and poor trim line.\(^4\)

**Neurogenic Pain.** This is the second most common type of residual-limb pain. All nerves that are transected develop a ball-like end of neural tissue called a neuroma. Neuroma pain has a sharp, shooting quality that can be produced by tapping over the area. This is known as Tinel’s sign. The neuroma may also generate pain spontaneously without any external stimulus.\(^4\)

**Arthrogenic Pain.** This is pain originating from a joint or the surrounding soft tissue. Joints commonly involved are the knee, hip, and sacroiliac joints. The surrounding ligaments, tendons, and synovium may also generate pain, particularly in older people.\(^4\)

**Sympathogenic Pain.** This type of pain, commonly referred to as reflex sympathetic dystrophy or chronic regional pain syndrome, has been reported in amputees.\(^{20,21}\) Symptoms in the acute phase include hyperthermia, hyperemia, edema, and hyperhidrosis. The pain is a diffuse, continuous burning ache. In the chronic phase, symptoms include pallor or cyanosis of the limb, hypothermia, induration, atrophic skin, decreased hair distribution, joint stiffness, and constant pain that is exacerbated by any stimulation of the affected area.\(^4\)

**Referred Pain.** This may result from radiculopathy, facet syndrome, sacroiliac dysfunction, piriformis syndrome, or myofascial pain. These musculoskeletal and neurologic conditions are more common in amputees owing to gait abnormalities that result in excessive biomechanical stress.\(^4\)

**Abnormal Tissue as a Cause of Pain.** The abnormal tissue may be bony exostoses, heterotopic...
ossification, adherent scar, ischemia, ulceration, hyperhidrosis, verrucous hyperplasia, or infection.4

Theories of Phantom Pain Production

Peripheral Theories

The central nervous system may misinterpret impulses generated from the residual limb as originating in the absent limb. Supporting evidence for central misinterpretation comes from 1) electrical stimulation of the stump, which causes increased phantom pain, and 2) local anesthesia of the stump, which eradicates phantom pain for the duration of its pharmacologic action.22

Neuromas from the cut ends of nerves in the stump have been noted to emit constant nerve impulses, which may be additional phantom pain generators. Occasionally, these spontaneous impulses have been reported to begin prior to the development of neuromas, thus explaining the immediate appearance of phantom pain noted in some amputees.22 These nerve impulses may be increased or decreased by cutaneous stimulation, which is probably the mechanism by which massage increases phantom pain in some individuals while decreasing it in others.5

Another peripheral theory suggests that non-nociceptive somatosensory receptors become damaged or sensitized, resulting in transmission of nociceptive impulses.23 This causes allodynia: the perception of pain during non-noxious stimulation. Nociceptive receptors may also become sensitized to the point where their pain threshold is significantly decreased, resulting in painful sensation during non-noxious stimulation.

Overproduction of sodium channels, as well as proliferation of α-adrenergic channels, calcium channels, and stretch-activated channels, has been noted in injuries to nerves. These may result in an ectopic depolarization site owing to membrane leakage of ions, stretch activation of channels, or adrenergic-receptor activation.24

Arguments against a peripheral mechanism include lack of consistent pain relief with dorsal ganglionectionomies, dorsal root resections, or spinal anesthesia.25-28

Spinal Theory

Noxious stimuli reach the spinal cord via fast-conducting myelinated A-delta fibers and slow-conducting unmyelinated C-fibers. A-delta fibers release excitatory amino acids, such as glutamate. The primary excitatory amino acid receptor in the dorsal horn of the spinal cord is the N-methyl-D-aspartate (NMDA) receptor. C-fibers release neurokinins, the principal one being substance P. Substance P causes depolarization of pain-specific secondary neurons in the dorsal horn and sensitizes other neurons to excitatory amino acids.29-30

With peripheral injury, excitatory amino acids and neurokinins are released at the same time, resulting in rapid depolarization of secondary nociceptive neurons and removal of the Mg2+-dependent block of further depolarization.29-30 The result is hyperexcitability and excitotoxicity from long-term depolarization and Ca2+ release. Death of inhibitory interneurons occurs, and secondary damage to the neuron itself results in synaptic remodeling. This cascade of events results in stimulus-independent depolarization and spontaneous pain generation.31-36

Central Theories

Melzack37 proposed the first central theory for phantom limb pain in 1971. He suggested that a schematic representation of a limb was built into the central nervous system owing to consistent sensory input over time. This representation could be thought of as an “engram” of the limb. Support for his theory has been provided by the anesthetization of peripheral nerves of an intact extremity, which results in the production of phantom sensation.38 Amputees experiencing phantom itching have also reported that “scratching” the pruritic area of the phantom limb can relieve the irritative sensation, further supporting the theory of a central schematic representation of the amputated limb.39 Further corroborative evidence comes from the higher prevalence of phantom pain following amputation of a painful extremity.2, 5, 40

The painful extremity may have created a painful central engram, which results in continuation of pain in the phantom limb following the amputation. Normalafferent signals originating in an extremity receive central inhibitory modulation via the brain stem. Another central theory suggests that a loss of peripheral afferent input from an amputated limb results in central disinhibition, causing pain magnification owing to neuronal sensitization.37, 41

Vascular Theory

Several studies have demonstrated that decreased blood flow to the residual limb increases certain types of phantom pain, including burning, throbbing, tingling, and cramping.16, 17, 42-44 Alterations in blood flow can be seen with residual-limb changes such as thickening or thinning of the residual limb’s skin, fluc-
tuation of edema, and changes in temperature. Muscle spasms may cause a “spike-like” pain in the residual limb and are often followed by an increase in phantom pain secondary to decreased residual-limb blood flow.

**Neuromatrix Theory**

In 1990, Melzack refined his central theory for phantom pain production into the “neuromatrix” theory. He proposed that the neuromatrix was a genetically determined framework of the physical self, created by complex communication between the somatosensory cortex and the thalamocortical, limbic, and occipital regions of the brain. This predetermined “substrate” of the physical self could be modified through sensory input, but could also act in the absence of sensory input, thus creating phantom sensation. The loss of sensory modulation may also result in an abnormal pattern in the neuromatrix, thereby causing phantom pain.45

Support for the neuromatrix theory includes the following observations: Patients with congenital limb amputations have reported the sensation of a normal or near-normal phantom limb.11, 12 Surgical lesions in the somatosensory cortex, including gyrectomies, typically do not result in the loss of phantom pain or phantom sensation.46 Patients with complete surgical transection of the spinal cord have reported phantom sensation in the paralyzed body parts, suggesting a supraspinal mechanism for phantom sensations.37 However, phantom pain and phantom sensation often appear to be generated independently. The relief of either phantom sensation or phantom pain rarely has an effect on the other.25, 47, 48

**Dynamic Reverberation Theory**

In 1994, Canavero49 proposed a theory he coined “dynamic reverberation.” He observed that focal lesions of the brain have resulted in resolution of phantom pain. The lesions were predominantly in the parietal cortex, the thalamus, or the corticothalamocortical fibers contralateral to the phantom pain. He noted several cases in which cortectomies resulted in relief of phantom pain and proposed that the failure of previous neurosurgical cortectomies to relieve phantom pain was due to insufficient amounts of cortical excision. Canavero theorized that phantom pain and phantom sensation were a result of a dynamic reverberation between the cortex and the thalamus that “may operate in the presence or absence of sensory activation.”49(p205)

It is evident from the above discussion that the exact etiology of phantom pain has yet to be determined and is probably multifactorial. Continued research to clarify the cause of phantom pain is needed.

**Treatments**

**Phantom Sensation**

Phantom sensation is treated with patient education both prior to and after surgery. The patient should be instructed that the incidence of phantom sensation following limb amputation is nearly 100%. Phantom sensation typically begins immediately postoperatively, feels very similar to the limb prior to surgery, and is nonpainful. Telescoping—the sensation that the distal phantom limb is moving more proximally—is a common phenomenon that may occur in the phantom limb over time. The intensity and character of phantom sensation may change, and this is a normal phenomenon.

**Residual-Limb Pain**

It is important to differentiate residual-limb pain from phantom pain, as residual-limb pain is far more responsive to treatment than phantom pain. A complete history should be obtained of the location, quality, severity, and radiation pattern of the pain, the factors that exacerbate and alleviate it, and its temporal character. A focused physical examination based on this information will often lead to the diagnosis. Physical examination should include inspection of the skin, muscle bulk and symmetry, posture, and gait as well as evaluation of the prosthesis for fit and wear. The residual limb should be palpated to locate areas of tenderness, scar adhesion, bony exostosis, and neuromas. The clinician needs to evaluate muscle strength for detectable weakness and joint range of motion to rule out contractures. Finally, the physician should check the patient’s sensation, as the lack of sensation predisposes skin to breakdown and infection.50

Aggressive postoperative pain management should include adequate pharmacologic treatment. Examples are oral opioid analgesics that are dosed on a time-contingent rather than a pain-contingent basis, a patient-controlled analgesia pump, epidural analgesia, peripheral nerve block, tramadol, nonsteroidal anti-inflammatory drugs, and acetaminophen. Nonpharmacologic pain management may include edema control by means of rigid postoperative dressing or stump wrapping, a transcutaneous electrical nerve stimulation unit applied to the skin roughly 1 cm away from the suture line,51 acupuncture,52, 53 ice ap-
plication, early mobilization, and massage. A thorough review of acute postoperative pain management has been presented by Carr et al.54

Common causes of prosthogenic pain include painful adductor roll on an above-the-knee amputee; volumetric changes in the residual limb, which result in poor prosthetic fit; lack of prosthetic relief over bony prominences; poor suspension, which results in pistoning; absence of proper inserts or cushions; improper prosthetic alignment, which results in abnormal gait patterns; and worn-out prosthetic equipment. Identification of the problem and proper prosthetic adjustment will relieve pain.55, 56

Surgical excision of painful neuromas is frequently successful.57 Neuromas may also be treated with chemical ablation by means of a phenol injection, pharmacologically with anticonvulsants, or with physical modalities such as electrical stimulation.4

Below-the-knee amputees commonly have pain in their knees, whereas above-the-knee amputees often have pain in their hips.4 The sacroiliac joint and lumbar spine may also be pain generators. Treatments include nonsteroidal anti-inflammatory drugs, ice or heat application, bracing of the joint, strengthening of surrounding musculature, stretching, avoidance of pain-generating activities, and education on proper gait and posture.55, 56, 58

Diagnosis of reflex sympathetic dystrophy or chronic regional pain syndrome is based on characteristic symptoms, physical findings, and increased static-phase uptake of the residual-limb bones on triple-phase bone scan.42 Early recognition is important for effective treatment.50, 60 Therapies include range-of-motion and strengthening exercises, heat or cold, contrast baths, edema control (elevation and graded compression), desensitization techniques, ultrasound, and application of a transcutaneous electrical nerve stimulation unit. Medications are often ineffective. Commonly used agents include nonsteroidal anti-inflammatory drugs, oral steroids, narcotic analgesics, α2-agonists, β-blockers, α-blockers, calcium channel blockers, tricyclic antidepressants, and anticonvulsants. Sympathetic blockade often relieves symptoms and can be performed by injection of the lumbar plexus or epidural space for lower-extremity reflex sympathetic dystrophy, or of the cervical plexus or stellate ganglion for upper-extremity reflex sympathetic dystrophy, or by using intravenous guanethidine in the affected extremity. Surgical sympathectomy may be performed for permanent treatment of those patients responsive to sympathetic block.50, 61, 62

Treatment of the referral source will alleviate the pain. Common causes and their treatments include the following:

1) Piriformis syndrome: This can be treated by heat application, stretching of external rotators, and strengthening of the hip girdle musculature.58

2) Radiculopathy: This may be treated conservatively with oral or epidural steroids; opiate analgesics; nonsteroidal anti-inflammatory drugs; centralization postural exercises (McKenzie), application of ice, heat, or both; programs to stabilize the back, neck, or both; and education on proper static and dynamic posture. Radiculopathies that do not respond to conservative treatment may require surgical intervention.63-65

3) Myofascial pain syndrome: Pain relief can be provided by a trigger-point injection of 1 mL of saline or lidocaine, or dry needling. The patient may also respond to spray and stretch techniques. Following pain relief, the patient should progress to a vigorous stretching and strengthening program along with the regular performance of cardiovascular exercise. The patient should also be instructed on correct dynamic and static posture. Sleep disturbance is a common finding associated with myofascial pain and often responds to tricyclic antidepressant medications.66, 67

The following are common abnormal-tissue diagnoses and their treatment:

1) Adherent scar: early postoperative scar mobilization by means of massage.55

2) Ischemia: antiplatelet medications, smoking cessation, revascularization, and adequate control of contributing disease states such as diabetes.

3) Ulceration: pressure relief and protection, adequate circulation and nutrition, adequate oxygen concentration, correction of contributing medical co-morbidities, and maintenance of a proper local wound-healing environment.50, 68-71

4) Infection: identification of the causative organism and appropriate antibiotic treatment. If the infection includes the bone, surgical excision of the infected bone is required for treatment.72

Phantom Pain

Current treatments for phantom pain can be divided into psychological, environmental, physical, pharmacologic, and neurosurgical categories.

Psychological Treatment. A psychological screen, such as the Minnesota Multiphasic Personality Index, may be used to help identify depression, situational anxiety, and hysterical reaction to loss of limb. Anxiety and depression have both been shown to magnify pain. Treatment of these psychological problems will help alleviate the amplification or exacerbation of phantom pain.18

Multiple studies on the efficacy of relaxation and biofeedback in the treatment of phantom limb pain.
have demonstrated a decrease in cramping or burning-type phantom pain. This is hypothesized to be due to muscle relaxation and vasodilation with improved circulation. In a case report of five patients, Sherman noted that all five patients experienced a significant reduction in phantom pain with the use of a combination of surface electromyographic biofeedback and relaxation techniques. However, the investigators did not report how long the pain relief lasted after each session, the ability of subjects to perform this technique on their own, or the long-term results. Further research on the role of relaxation and biofeedback treatment is required.

Preamputation counseling regarding body image and limb loss should be performed. The patient will proceed through the normal grieving process of denial, bargaining, anger, depression, and acceptance following the loss of the limb. Allowing the patient to identify and face this loss will help facilitate emotional well-being and possibly decrease the incidence of phantom pain.

Hypnosis has also shown some success in control of phantom pain, but its role in the treatment of phantom limb pain requires further clarification.

Environmental Treatment. For environmental treatment of phantom limb pain, consider having the patient keep a log for 1 week charting the phantom pain as it relates to weather, food, and physical stress. Pain that increases with weather changes should receive a trial of nonsteroidal anti-inflammatory drugs. The patient should discontinue foods that exacerbate symptoms and change physical behaviors that increase pain levels.

Physical Treatments. These include acupuncture, galvanic electrical stimulation, ultrasound, massage, transcutaneous electrical nerve stimulation, and rigid postoperative dressings for edema control and desensitization. Acupuncture has been shown to provide mild-to-moderate temporary reductions in phantom pain. Galvanic electrical stimulation and ultrasound have both shown predominantly temporary reductions in phantom pain, although there have been a few case reports of permanent pain control. Heat produces mild temporary analgesia in 50% of phantom pain cases. Residual-limb desensitization through massage may result in temporary mild-to-moderate phantom pain reduction in selected cases. However, there have been reports of permanent phantom pain reduction with residual-limb desensitization techniques. All of the above responses to physical treatments were based on a survey of phantom pain treatments among US veterans, and further controlled trials are required to better delineate their respective efficacies.

Transcutaneous electrical nerve stimulation has proven to be the most consistent physical modality for control of phantom pain. Response rates range from 45% to 65%. Its simplicity and effectiveness make it an attractive treatment choice. However, variability in long-term efficacy has been reported.

Use of rigid postoperative dressings and aggressive edema control are important to minimize postoperative residual-limb pain, thus reducing the later development of pain syndromes. These measures also facilitate early prosthesis fitting and use, which has been associated with a decreased incidence of phantom pain.

Pharmacologic Treatments. These include narcotic analgesics, β-blockers, anticonvulsants, baclofen, tricyclic antidepressants, neuroleptics, calcitonin, mexiletine, epidural anesthesia, regional anesthesia, tizanidine, ketamine, and capsaicin cream (Table 1).

Narcotic Analgesics. These have been shown to be of little benefit in the long-term treatment of phantom pain. However, in combination with antidepressants, their effectiveness may be improved. Typically, narcotic use should be restricted to acute episodes of moderate-to-severe pain, such as postoperative pain.

β-blockers. Preliminary reports suggest that β-blockers such as propranolol may have a role in the treatment of phantom pain. Proposed mechanisms include improved blood flow as well as central effects on serotonin levels.

Anticonvulsants. Anticonvulsants such as carbamazepine, phenytoin, valproic acid, and clonazepam have all been reported to improve phantom pain with...
variable results.89, 90, 91 The new anticonvulsant gaba- 
pentin has the advantage of a low side-effect profile 
and does not require monitoring of blood levels, but 
studies on its efficacy in phantom pain treatment 
have yet to be performed.

_Baclofen._ Another centrally acting agent that may 
be helpful is baclofen, a γ-aminobutyric acid ana-
logue most commonly used for the treatment of spas-
ticity.14 Baclofen has been used to treat many other 
pain syndromes, including trigeminal neuralgia,89 
and was successfully used by Iacono et al14 to treat two 
patients with phantom pain.

_Tricyclic Antidepressant Medications._ Tricyclic 
antidepressant medications, such as imipramine and 
amitriptyline, increase central levels of serotonin, 
thereby activating descending pain-inhibitory neu-
rons and resulting in decreased afferent pain impulses 
from the dorsal horn cells.80, 91 They also affect lev-
els of dopamine and norepinephrine, which play a 
role in the treatment of depression.80 Depression is 
often present in patients with chronically painful 
conditions. In addition, chronic pain patients may 
have sleep disturbances, which may be amenable to 
tricyclic antidepressant treatment.82

_Neuroleptic Medications._ Neuroleptic medica-
tions, such as phenothiazines, have been used for re-
fractory cases of phantom pain with reported re-
response rates of between 40% and 100%.93-96 The 
proposed mechanism of action by which neuroleptic 
edications alter phantom pain perception is an al-
teration in central interpretation of painful stimuli.

_Calcitonin._ A double-blind, placebo-controlled 
study of intravenous calcitonin noted excellent long-
term results in the treatment of phantom pain.97 An-
other study showed an immediate response of phan-
tom pain to calcitonin in nine of ten patients, with 
pain relief lasting between 2 hours and 3 months.98 
The exact mechanism of action by which calcitonin 
provides pain relief is not known. The analgesic ef-
fects of calcitonin can be reversed by serotonin-
blocking agents, and calcitonin receptors in the cen-
tral nervous system are near areas rich in serotonin, 
such as the hypothalamus and limbic system.99, 100 
This suggests that serotonin may play a role in the 
phantom pain relief caused by calcitonin administra-
tion. Significant side effects such as dysesthesia, nau-
sea, and vomiting have been noted.98 The most effec-
tive dosing regimen has yet to be determined.

_Mexiletine._ An open-label study of mexiletine was 
performed by Davis101 in 1993. Eighteen of 31 pa-
tients responded to mexiletine alone, while 11 other 
patients responded to a combination of mexiletine 
and clonidine. Two patients did not respond to either 
regimen, and three patients discontinued mexiletine 
treatment owing to nausea. The most likely mecha-
nism of action by which mexiletine reduces phantom 
pain is through blockade of the sodium channels in 
hyperexcitable (sensitized) neurons. This results in 
suppression of pain-generating foci.

_Epidural Anesthesia._ Preoperative pain control 
by means of epidural anesthesia has been shown in 
several studies to significantly reduce the incidence 
of phantom pain.102-104 The medications used for 
epidural anesthesia in phantom pain studies have in-
cluded morphine, bupivacaine, clonidine, diamor-
phine, and fentanyl. The proposed mechanism by 
which phantom pain is reduced with preoperative 
pain control is reduction of central sensitization by 
peripheral noxious stimuli. The time period for the 
initiation of epidural anesthesia prior to surgery and 
the duration of treatment have varied across studies. 
Further research to delineate the most efficacious 
treatment protocol needs to be performed.

Epidural anesthesia has also been successfully 
used to treat established phantom pain.305, 106 A case 
report by Jacobson and Chabal106 demonstrated 
phantom pain relief with epidural anesthesia in a pa-
tient recalcitrant to many other pharmacologic treat-
ment methods. Intravenous administration of similar 
drug combinations has not produced the same pain 
relief noted for the epidural route.105

Regional Anesthesia. Regional anesthesia (such as 
fusions of local anesthetic into the brachial plexus, 
sciatic nerve, or tibial nerve) has been performed 
with varying degrees of success.107, 108 Birbaumer et 
al108 noted a significant reduction of phantom pain in 
three of six patients undergoing regional anesthesia. 
No reduction in pain was found in the remaining 
three patients. Immediate postoperative perineural in-
fusion of bupivacaine for 3 days has not been shown 
to reduce the incidence of phantom pain.108

_Tizanidine._ Tizanidine, a new α2-adrenergic re-
ceptor agonist used predominantly for the treatment 
of spasticity, was studied for its effects on phantom 
pain by Vorobeichik et al.110 In a small double-blind, 
placebo-controlled study, significant pain relief was 
demonstrated in 13 of 14 patients with phantom pain 
who received tizanidine. These are promising results, 
but further study is required.

_Ketamine._ This NMDA receptor antagonist has 
been used intravenously to treat phantom pain. In a 
study by Nikolajsen et al,111 11 of 11 patients re-
sponded to treatment with intravenous ketamine. 
However, 9 of the 11 patients reported significant 
side effects. While NMDA receptor antagonist thera-
py may eventually play a significant role in phantom
pain treatment, significant side effects currently limit its widespread use.

Capsaicin Cream. Two case reports have been published on the efficacy of capsaicin cream in the treatment of phantom limb pain. Rayner et al.\textsuperscript{112} reported phantom pain reduction with capsaicin cream, while Weintraub et al.\textsuperscript{113} reported no pain relief. Further studies using a larger number of patients and a control group need to be performed prior to determining capsaicin’s role in the treatment of phantom pain.

Neurosurgical Treatments. These include excision of painful neuromas, sympathectomy, dorsal column stimulators, dorsal root entry zone lesions, and deep brain stimulators. It should be noted that neurosurgical treatment of phantom pain should be attempted only after extensive pharmacologic and nonpharmacologic therapies have failed to relieve phantom pain.

Surgical Excision or Revision of Painful Neuromas. This treatment often leads to a reduction in residual-limb pain, but not in phantom pain.\textsuperscript{52}

Sympathectomy. This may be appropriate for patients with documented reflex sympathetic dystrophy who have had excellent short-term relief with four to six sympathetic blockades, but who have not achieved long-term results.\textsuperscript{114}

Dorsal Column Stimulators. These, also known as spinal stimulators, are based on the gate-control theory presented by Melzack and Wall in 1965.\textsuperscript{115} The spinal stimulator causes depolarization of the fibers located in the dorsolateral funiculus of the spinal cord, which are responsible for descending supraspinal pain suppression.\textsuperscript{13} Other mechanisms are probably involved, but they are poorly understood. A few studies have shown good results, but one study showed spinal stimulators to be no better than a placebo.\textsuperscript{78, 116-118}

Dorsal Root Entry Zone Lesions. These are radiofrequency thermal lesions placed in the substantia gelatinosa of the dorsal horn. This is an area of the spinal cord where disinhibited or sensitized neurons from deafferentation are thought to be located. These lesions have been used with success for treatment of nerve root avulsion injuries resulting in deafferentation pain, but have shown only marginal results when used to treat phantom pain from amputation.\textsuperscript{48, 119-121}

Deep Brain Stimulation. Patients with severe, intractable phantom pain may be candidates for deep brain stimulation. Mundinger and Neumuller\textsuperscript{78} found that stereotactically placed electrodes in the sensory nucleus of the thalamus or periventricular gray matter or internal capsule provided significant pain relief in 26 of 30 patients.

Conclusion

Health-care providers must be well versed in the different kinds of sensations experienced by amputees. A complete history and physical examination will help differentiate among phantom sensation, phantom pain, and residual-limb pain. Phantom sensation does not require any intervention other than patient education. The most treatable form of postamputation pain is stump pain, which should always be an important part of the differential diagnosis.

The etiology of phantom pain continues to be elusive. Several recent theories of phantom pain etiology have been presented, but the exact cause is likely to be multifactorial and may differ from patient to patient, as manifested by the variable responses of patients to treatment.

Therapeutic regimens have displayed some promising advances in recent years. A multidisciplinary team approach to patient care is important. The patient should receive preoperative counseling and education as preparation for limb loss and phantom sensation. A behavioral screen to identify possible risk factors for phantom pain should be performed and appropriate interventions instituted. Resources should be available to facilitate the lifestyle modifications required by the amputee, such as vocational retraining and alterations in home or work environment. If patients are medically and physically able, they should begin a preoperative physical conditioning program to help facilitate their transition to postoperative independence. Preoperative pain management by means of epidural anesthesia should be performed. Aggressive postoperative pain management should also be provided, and edema should be controlled with early prosthesis fitting.

If phantom pain does develop, rapid and aggressive treatment should be instituted. Biofeedback and relaxation techniques may provide some relief, and transcutaneous electrical nerve stimulation, desensitization, and early prosthetic use may also be of benefit. Tricyclic antidepressants, anticonvulsants, and baclofen may be tried, but have variable effectiveness. β-Blockers (propranolol) and α₂-adrenergic agonists (ti- zanidine and clonidine) have shown promise in small trials and have a more benign side-effect profile compared with many other medications used to treat phantom pain. Other promising medications are calcitonin and mexiletine. However, exact dosing regimens for these medications have yet to be determined, and potential adverse effects must be kept in mind.

For patients recalcitrant to conservative measures, neurosurgical procedures including dorsal root entry zone lesions and spinal stimulators are op-
tions. Patients with intractable pain after the above measures are tried may be candidates for deep brain stimulation.

Maximizing functional outcome and improving the quality of life should always be the therapeutic goal in the treatment of amputee patients. This can be accomplished through a multidisciplinary team approach to the treatment of phantom sensation, phantom pain, and residual-limb pain.

References