One of the most challenging clinical issues the dentist confronts is the patient with persistent orofacial pain without obvious proximate physical cause. Patients with persistent pain often seek consultation from many clinicians and undergo multiple unnecessary procedures before receiving a correct diagnosis and appropriate treatment. Clinicians unfamiliar with neuropathic pain may become frustrated and, with the best of intentions but limited information, provide familiar but inappropriate treatment directed toward a dental or other somatic pain. The spectrum and prevalence of orofacial neuropathic pains is such that every dentist will certainly encounter patients with neuropathic pain. Therefore, to avoid unnecessary and inappropriate diagnosis and treatment, the dentist must gain familiarity with the pathophysiology, presentation, diagnosis, and treatment of orofacial neuropathic pain.

By definition, neuropathic pain is nonadaptive and does not contribute to healing, such as would be the case with pain attributable to tissue inflammation, where pain results in adaptive behaviors, such as use limitation, guarding, rest, and avoidance, which contribute to healing. Neuropathic pain persists without real or potential benefit, resulting only in unnecessary suffering.

**Somatic versus neuropathic pain**

**Somatic pain**

As a first step toward understanding neuropathic pain it is important to recognize the fundamental difference between somatic and neuropathic pain. Somatic pain always results from stimulation of nociceptors, owing to tissue injury. Nociceptors are the sensory receptors specialized for detecting noxious thermal, mechanical, or chemical stimuli resulting from tissue injury. The neuroimmune interactions following tissue injury result in nociceptor sensitization such that the threshold for activation is reduced and the magnitude of response is increased. Thus, light touch in an area of inflammation or warm water in contact with burned skin or mucosa becomes painful, not because the physical energy itself is noxious
but because the nervous system response is heightened. Primary hyperalgesia is the term used to describe the increased perception of a painful stimulus following receptor sensitization; it is a hallmark of somatic pain. Allodynia refers to the perception of pain in response to a non-noxious stimulus; this too is often present during primary hyperalgesia. Most somatic pains end when the underlying tissue injury and inflammation resolves.

**Neuropathic pain**

Neuropathic pain is fundamentally different from somatic pain in that nociceptor stimulation is not necessary. Whereas tissue and nerve injury may initiate processes that lead to pain, neuropathic pain persists once the initial injury heals. Herein lies the diagnostic challenge, since in most cases of neuropathic pain there is no evidence of ongoing tissue injury or inflammation to “substantiate” the pain, often leading to treatments directed at disease that does not exist (ie, endodontic therapy without pulpal injury, tooth extraction without odontogenic disease). Allodynia and mechanical hyperalgesia are common features of neuropathic pain: the patient experiences increased pain to noxious stimuli as well as pain to non-noxious stimulation. Two general types of neuropathic pain exist: paroxysmal pain and continuous pain. Paroxysmal pain refers to sudden, brief (seconds to minutes) but intense pain, which may be spontaneous or provoked by light touch or movement in the affected area. Continuous neuropathic pain has a constant burning or stinging quality that may have periods of greater or lesser intensity. Unlike somatic pain, paroxysmal neuropathic pain is characterized by pain-free intervals and, therefore, does not exhibit the same reliable provocation of pain upon stimulation. Furthermore, neuropathic pain does not necessarily occur in the area that evokes the pain when stimulated; that is, there can be referral of the pain sensation to areas outside the stimulation zone.

A final note regarding the origins of sensation and perception is required before discussing specific neuropathic pain illnesses. Certainly, the vast majority of sensory perceptions are evoked by and accurately represent the actual physical stimulus delivered. However, one must realize that all perception is a product of neural activity in the central nervous system (CNS). Although most times the evoked CNS neural activity appropriately encodes a physical stimulus, it is certainly the case that CNS activity in the absence of an externally applied physical stimulus can lead to a sensory experience. It is well known that electrical stimulation of the CNS can produce vivid sensory perceptions in the absence of peripheral stimulation. Pathologic processes that result in inappropriate CNS activity can produce sensory perceptions that have no physical correlate, yet they can be as real and valid as the sensory perception evoked by a physical stimulus.

A dramatic illustration of the neurogenous origin of perception is the common experience of phantom sensations and pains that follow amputation, where there no longer exists a peripheral substrate (ie, arm, leg) for experiencing the sensation. Bear in mind that the most common amputation performed is pulp extirpation and tooth extraction, both of which can result in neuropathic phantom sensation and pain in a denervated or missing tooth. The unorthodox yet undeniable fact remains that one does not need to have a body part to experience a sensation or pain from the corresponding region, and there exist neural processes that can initiate and sustain a real perception in the absence of a physical stimulus. Thus, the practitioner must accept what the patient says he or she is feeling as a real sensory experience with a physiologic, albeit not necessarily physical basis. Treating the neuropathic pain condition as though the pain originates in the structures where the pain is perceived fails to recognize the neurogenous nature of neuropathic pain and often leads to inappropriate and ineffective treatment. Instead, successful treatment is that which focuses on eliminating or controlling abnormal neural activity.

**Orofacial neuralgias**

**Trigeminal neuralgia**

Clinical features

Trigeminal neuralgia is an excruciating, debilitating orofacial pain illness largely recognized as one of the most painful human conditions. It is also known by the name tic douloureux owing to the facial expression or wince that often accompanies the painful episode. Trigeminal neuralgia is a rare disorder, with an overall incidence of 3 to 5 persons per 100,000 (and an increased risk in the elderly where incidence rises two- to threefold to 6 to 12 persons per 100,000). Although rare, trigeminal neuralgia assumes a place of prominence in dental medicine because many patients with trigeminal neuralgia believe the pain may be tooth-related and seek initial care from the dentist. The pain is described as stabbing, shooting, electric shock-like pain lasting seconds to minutes. Most times the patient is aware of the trigger for pain, such as light touch to an intra- or extraoral region, or facial or tongue movement. Thus, trigeminal neuralgia is the quintessential neuropathic pain, characterized by profound allodynia. The pain often radiates to areas outside the trigger zone. The frequency is variable, from several episodes daily to every few months; in rare and progressive cases the pain may become continuous. The pain is almost always unilateral and occurs nearly equally in the maxillary and mandibular trigeminal divisions, less commonly, in the maxillary division.
ophthalmic division. Trigeminal neuralgia occurs nearly equally among males and females, though some reports have found slightly higher rates among females.

Trigeminal neuralgia may be primary or secondary. Secondary trigeminal neuralgia occurs because of some identified abnormality, such as an intra- or extracranial tumor or other space-occupying lesion, multiple sclerosis (MS), or trauma. Primary trigeminal neuralgia occurs in the absence of an identified cause; most cases of trigeminal neuralgia are primary. Primary trigeminal neuralgia usually occurs in individuals over 50 years of age, whereas secondary trigeminal neuralgia usually occurs in younger individuals. Thus, the suspicion for an underlying illness, such as tumor or multiple sclerosis, is increased in younger patients with trigeminal neuralgia, and their evaluation must include computerized tomography (CT) or magnetic resonance imaging (MRI) of the head and brain to identify related pathology.

Etiology
Most cases of trigeminal neuralgia are primary in nature, without an identified underlying cause. Although a universal etiologic theory for trigeminal neuralgia does not exist, there is little disagreement that it is a neuopathic pain disorder resulting from altered sensory processing either in the trigeminal ganglion or the central trigeminal neuraxis. Detection and encoding of the light touch stimulus that provokes the pain is apparently normal at the sensory receptor level, with a loss of modality properties (light touch leading to pain sensation) occurring at or proximal to the trigeminal ganglion. A commonly accepted but not proven etiology is the presence of abnormal vascular anatomy, most commonly the superior cerebellar artery, which presses against the trigeminal root in the posterior cranial fossa. Neurosurgical correction by microvascular decompression has been widely used for correction of the vascular abnormality. Demyelination has often been suggested as the underlying pathology that leads to abnormal electrical excitability and pain, although sound evidence to support this theory is lacking.

Secondary trigeminal neuralgia develops as a result of an underlying disorder, such as intra- or extracranial tumor or other space-occupying lesion, MS, or trauma. Common intracranial tumors that can cause trigeminal neuralgia include pituitary adenoma, meningioma, glioma, and acoustic neuroma. In such cases, the underlying disorder presumably leads to ectopic electrical activity caused by direct pressure or demyelination. It is not clear, however, why the pain is episodic even though the underlying pathology is constant. Approximately 5 to 10% of patients with MS develop trigeminal neuralgia, which may be the initial symptom of undiagnosed MS. Whenever trigeminal neuralgia develops in a younger individual, the suspicion for underlying disease should be increased and appropriate diagnostic imaging tests should be ordered.

Diagnosis
Trigeminal neuralgia is a clinical diagnosis based almost exclusively on the history and physical examination; imaging studies may further identify underlying disorders. Paroxysmal unilateral pain described as sharp, stabbing, or electric-like with pain-free intervals and an identified trigger are the essential features. The possibility for local somatic disease (ie, odontogenic) should be carefully evaluated, though odontogenic somatic pain is unlikely to be characterized by intermittent episodes of pain. A complete cranial nerve examination should be performed, and suspicion for trigeminal neuralgia secondary to tumor, vascular abnormality, or MS should be increased when there are other abnormalities on the neurologic examination. Because the condition is intermittent and paroxysmal, the physical examination is typically completely normal. Trigeminal sensory thresholds are generally normal and symmetric, except during a pain episode when there exists profound allodynia. There are generally no signs of somatic or inflammatory injury. Diagnostic imaging (CT or MRI) when multiple sclerosis is suspected should be performed for all patients with trigeminal neuralgia, and especially those who develop symptoms before 50 years of age.

Do not treat what has not been diagnosed. Adherence to this simple principle avoids the unfortunate but not uncommon experience of many patients with trigeminal neuralgia who receive inappropriate treatment directed toward an odontogenic source that does not exist. Although certainly there are some instances in which it is difficult to exclude the possible contribution of coexisting dental disease, bear in mind the fundamental differences between odontogenic (somatic) and neuropathic pain. If the pain is believed to be caused by an odontogenic disease, then generally speaking the pain will be more constant in nature, respond faithfully to provocation by mechanical or thermal stimulation, and be localized to the region of presumed pathology. If the pain is caused by trigeminal neuralgia, virtually none of those features of somatic pain will exist, rather the pain will be intermittent, paroxysmal, and outside the trigger or provocation zone.

Treatment
Several medical and surgical modalities of treatment exist for trigeminal neuralgia; all therapies are directed toward reducing nerve excitability. Medical therapy is the preferred initial treatment for those who can tolerate the medications. Membrane-stabilizing medications, such as carbamazepine, gabapentin, valproic acid, phenytoin, and baclofen are commonly used alone or in combination. These medications all act to reduce nerve
excitability by modulating conductance of ions across the excitable nerve membrane. Medications should be prescribed only by those clinicians experienced with their use, since all have side effects and adverse reactions, and some require hematologic monitoring. Medical treatment provides complete or acceptable levels of relief for approximately 75 to 80% of patients. Some patients enjoy complete remission, and a minority may become unresponsive after prolonged medical therapy. Surgical therapies exist for those patients who cannot tolerate, become refractory to, or do not respond initially to medical therapy.

An invaluable class of medications for the treatment of neuropathic pain in general are the tricyclic and heterocyclic antidepressant drugs, most notably amitriptyline and nortriptyline. These drugs are used alone or in combination with membrane-stabilizer medications, but at doses far below those used to treat clinical depression or other mood disorders. Although their exact mechanism of action for providing relief of neuropathic pain is not known, it appears that their modulation of noradrenaline neurotransmission at segmental (spinal cord and brain stem) as well as supraspinal levels reduces neuronal excitability and pain perception. It is clear that these drugs used in the dose range for neuropathic pain are not treating a clinical depression or other primary mood disorder.

Minimally invasive treatments for trigeminal neuralgia include percutaneous glycerol or alcohol injection or radiofrequency neurolysis directed toward the affected trigeminal division. These neuroablative procedures are performed by the anesthesiologist or neurosurgeon under fluoroscopic imaging for guidance and generally aim to inactivate, for varying periods of time sensory signals from the trigger zone; a common side effect is variable levels of anesthesia in the territory supplied by the treated nerve. Most recently, preliminary results using minimally invasive stereotactic gamma radiation (“gamma knife”) have demonstrated excellent relief. The percutaneous and stereotactic radiosurgery techniques provide relief for about 75% of patients, especially those who have failed medical therapy; these procedures may need to be repeated months to years later if symptoms recur. Finally, microvascular decompression is a cranial neurosurgical procedure to reposition an aberrant blood vessel, usually the anterior superior cerebellar artery. As a neurosurgical procedure, it has the risks of hearing loss, corneal anesthesia, cerebral embolism, and facial nerve injury, among others. However, for patients who have failed other forms of treatment, it also offers an approximately 75% success rate. Trigeminal neuralgia secondary to intra- or extracranial tumor or attributable to MS is treated by addressing the underlying disorder. However, many patients require the additional use of membrane-stabilizing medications or tricyclic or heterocyclic medications.

**Glossopharyngeal neuralgia**

**Clinical features**

Glossopharyngeal neuralgia is a neuropathic pain that shares many of the features of trigeminal neuralgia, with a few notable exceptions. The pain location is in the distribution of the glossopharyngeal nerve, specifically the posterior tongue and lateral oropharynx. The pain is less intense than that of trigeminal neuralgia, though still paroxysmal and episodic in nature, and is provoked by swallowing or contact with the mucosa overlying the region innervated by the glossopharyngeal nerve. Glossopharyngeal neuralgia is a rare disorder, affecting approximately 0.5 to 1 person per 100,000.

**Etiology**

Glossopharyngeal neuralgia, more so than trigeminal neuralgia, lacks a unifying etiologic theory. Most recognize underlying disease processes similar to those proposed for trigeminal neuralgia, namely tumors and vascular abnormalities that result in nerve compression and ectopic nerve impulses, demyelination, and trauma.

**Diagnosis**

The diagnosis of glossopharyngeal neuralgia, much the same as for trigeminal neuralgia, is a clinical diagnosis based on the history and examination. The possibility for an odontogenic source is less likely, owing to the anatomic region involved. A complete cranial nerve examination is essential for detecting other abnormalities that might support an underlying illness, such as MS or a tumor. Computed tomography and MRI are appropriately prescribed to detect related intra- or extracranial disease.

**Treatment**

Glossopharyngeal neuralgia is responsive to the same medical therapies used to treat trigeminal neuralgia. Minimally invasive and cranial neurosurgical procedures are seldom used owing to more limited accessibility to the glossopharyngeal nerve. As in trigeminal neuralgia, glossopharyngeal neuralgia secondary to intra- or extracranial tumor or attributable to MS is treated by addressing the underlying disorder. However, many patients require the additional use of membrane-stabilizing medications or tricyclic or heterocyclic medications.

**Postherpetic neuralgia**

**Clinical features**

Unlike trigeminal and glossopharyngeal neuralgia, postherpetic neuralgia (PHN) is not a paroxysmal neuropathic pain, rather it is a continuous burning or stinging neuropathic pain that persists for more than 3 months in the distribution of a previous outbreak of herpes zoster,
or shingles. Postherpetic neuralgia shares with other neuropathic pains the features of hyperalgesia and allosthenia. Except in the rare case of herpes sine zoster, or zoster reactivation without associated lesions, the vast majority of patients report an antecedent episode of shingles. Since herpes zoster, like other human herpes viruses, is a neurotropic DNA virus, it remains dormant in the DNA of primary sensory ganglia following primary infection by varicella zoster (chicken pox). Subsequent viral reactivation is associated with a painful vesiculoulcerative rash on the skin or mucosa, corresponding to the sensory dermatome of the involved nerve. The condition is usually unilateral, though it may disseminate by the blood in immunocompromised hosts. Only about 20% of shingles cases affect the trigeminal nerve, involving both intra- and extraoral dermatomes; approximately 80% of cases affect the spinal nerves.

Most cases of herpes zoster affect individuals over 60 years of age, with an estimated prevalence as high as 24% in that age group. The estimated prevalence of PHN following herpes zoster among patients over 60 years of age is between 15% and 40%, an approximately 15- to 25-fold increased risk compared to patients younger than 30 years. Thus, the risk for, and need to prevent PHN increases significantly with age. Postherpetic neuralgia is more common among females.

Etiology
Following viral reactivation, the herpes zoster virus is transported through the neuronal axoplasm to the peripheral afferent terminals, where its release initiates an intense inflammatory response resulting in the clinical lesion of shingles. During the approximately 2-day period it takes for the virus to travel the distance of the trigeminal nerve, there is an intense neuritis that may be associated with a tingling or burning prodrome before lesions develop. Several reports have demonstrated neuronal degeneration of affected primary afferents in the spinal cord, resulting in a loss of primary fibers as well as degeneration of local and second-order neurons. These degenerative changes are believed to play a major role in the establishment of PHN that persists as a neuropathic pain long after the zoster lesions have healed.

Diagnosis
Postherpetic neuralgia is generally a clinical diagnosis based on the history and examination, which reveal antecedent zoster with burning, hyperalgesia, and allodynia in the affected dermatome. Since no virus exists in the painful region after the zoster lesions have healed, there is little benefit to viral culture or evaluation of serum antibody titers to herpes zoster.

Treatment
Since PHN occurs most commonly in patients over 60 years of age, this age group should receive the most aggressive treatment at the earliest opportunity. Treatment outcome is dramatically improved with early treatment: the risk for developing permanent PHN doubles when pain persists for more than 6 months. Any patient over 60 years of age who develops shingles should be treated with both antiviral medication (acyclovir, famciclovir) and a tricyclic antidepressant (amitriptyline, nortriptyline) to reduce the risk for PHN since preemptive treatment with a tricyclic antidepressant reduces by 50% the risk of developing PHN. Unfortunately, the dentist rarely has the opportunity to contribute to preemptive treatment, since patients most often seek care from their physician for shingles. Nonetheless, tricyclic antidepressant medications should be prescribed as soon as possible during the course of PHN. Corticosteroid medications have also been prescribed during the acute phase of zoster to reduce neuritis, though its efficacy in preventing PHN has been inconclusive.

Capsaicin cream (0.025% and 0.075%) has been shown to be an effective topical medication for the relief of PHN when applied to the painful region. Application 2 to 3 times daily of capsaicin depletes substance P, a neuropeptide contained in nociceptive C-fibers that contributes to neuropathic inflammation and pain. Initial application of capsaicin may result in a burning sensation, but this is diminished after repeated use during the first 48 to 72 hours.

Nerve injury and neuroma pain

Clinical features
Nerve injury associated with tissue injury results in a complex series of bidirectional events between the nervous and immune system. Whereas this response is intended to promote healing, it may also result in pathologic events that lead to persistent neuropathic pain. These events may include functional changes in CNS and peripheral sensory processing (neuroplasticity) as well as neuroma formation. A neuroma is an incomplete or failed attempt at nerve repair following injury to a peripheral nerve, resulting in a disorganized nerve fiber that is focally electrically excitable. The pathologic sensitization of the injured peripheral nerve or CNS results in both peripheral and CNS hyperexcitability, which are manifest as focal allodynia and mechanical hyperalgesia at the site of injury.

What sets nerve injury and neuroma pain apart from the neuralgias is the provocation of pain upon stimulation of a discrete region innervated by the injured nerve. Whereas the neuralgias demonstrate episodic pain, pain-free intervals, and periods of normal stimulus-response function between attacks, neuroma and nerve injury pain most often result in constant allodynia and mechanical hyperalgesia in a discrete zone supplied by
the injured nerve. Rarely is there a palpable or otherwise detectable mass corresponding to the location of a neuroma. Neuroma pain is usually bright, sharp, and well localized but may also result in radiating pain sensations as well as continuous burning pain that spreads beyond the immediate injured region.

Etiology
Although knowledge of the full spectrum of events that can occur following nerve injury continues to expand at a rapid pace, several relevant events are known at this time. Within moments of tissue and nerve injury, a complex series of neuroimmune events occur that can: (1) sensitize the injured nerve, (2) lead to neurogenic inflammation and promote further leakage of proinflammatory mediators from the injured blood vessels, (3) contribute to neuroproliferative events that may contribute to neuroma formation, and (4) result in functional and phenotypic changes in primary and second-order neurons such that these neurons change their future excitability and responsiveness. Together, the pathologic events may result in CNS neuroplasticity and hyperexcitability that sustain a neuropathic pain condition. It is not clear why literally millions of patients undergo millions of invasive procedures every day yet only a small portion develop postprocedure neuropathic pain. Certainly, there are multiple factors that come to bear, none of which are sufficiently well understood to develop a working theory. It is interesting to note that there exist engineered strains of mice that predictably respond to nerve injury and involve neuroproliferative events that may contribute to neuroma formation and promote further leakage of proinflammatory mediators. Strains of mice that predictably respond to nerve injury continue to expand at a rapid pace, several relevant events are known at this time.

Diagnosis
Nerve injury and neuroma pain most often are associated with an identifiable antecedent injury. However, the nature and extent of that injury can vary. Although a rare event, even minor trauma from periodontal scaling, pulp extirpation, and minor incision can potentially lead to neuropathic pain. There must be a careful search for focal mechanical hyperalgesia and allodynia; this can be difficult and be associated with an area as small as 2 mm². Identification of a reliably sensitive focal area is highly suggestive of a neuroma. A small amount of local anesthesia applied to the painful focus eliminates the pain and further supports the essentially peripheral nature of the problem. However, persistence of pain after local anesthesia does not exclude the existence of a neuroma, but may indicate the coexistence of pathologic neuroplastic changes in the CNS that contribute to the pain experience.

Treatment
When the injury involves a large-caliber nerve (inferior alveolar, lingual) and the precise location of the presumed neuroma can be reasonably well determined, microsurgical repair is an option. However, such localization and involvement of a larger nerve is uncommon, making surgical repair a less effective treatment alternative. Furthermore, nerve injury and neuroma pain that persists for a long time (more than 6 mo) is less amenable to a favorable surgical outcome. Locally applied capsaicin cream can be an effective treatment for focal nerve injury pain. Use of capsaicin intraorally may require fabrication of a stent that can keep the cream in contact with the mucosal surface and minimize leakage throughout the mouth. The cream should be massaged into the painful area three times daily, then covered with a stent when possible for approximately 20 minutes. Although there are a few reports of repeated local anesthetic injection with or without corticosteroid (which has been shown to reduce neuroma excitability), definitive long-term data are lacking. Likewise, several topical formulations of membrane-stabilizer and N-methyl-D-aspartate (NMDA) antagonists have been reported in isolated cases and small case series, again without definitive long-term data. The use of tricyclic antidepressant medications as neuropathic analgesics often provides additional relief.

Phantom tooth deafferentation pain
Clinical features
Phantom tooth pain (PTP) is a condition of persistent pain in the teeth, face, or alveolar process that follows pulp extirpation, apicoectomy, or tooth extraction. Several reports have demonstrated that approximately 3 to 4% of patients undergoing endodontic therapy have persistent, unexplained pain or unpleasant sensations in the treated tooth. The term phantom tooth pain was first coined in 1978, though the condition has been recognized by different terms for many decades. The patient with PTP is the one most likely to have undergone multiple conventional and surgical endodontic treatments as well as tooth extractions in a continued attempt to relieve the phantom pain. This also is the patient most likely to be labeled by the clinician as having a psychogenic pain. Recognizing the condition as a neuropathic pain rather than a somatic or psychogenic pain should immediately prevent such treatment, since somatic pain would not move from one tooth to the next or persist after the nerve has been amputated. Patients with PTP are often diagnosed incorrectly with atypical facial pain (see Chapter 33).

The patient with PTP usually describes a constant dull, deep, aching pain with occasional spontaneous sharp pain; there is no refractory period. The pain is experienced in a tooth that is denervated by root canal therapy or has been extracted. The phantom sensation...
is in the missing tooth itself, rather than in the edentulous alveolar ridge, which is more accurately described as an intraoral stump pain. The patient may also experience perverted sensations of tooth size, shape, or location. As treatment is directed toward the “symptomatic” tooth, the symptoms often spread or move to adjacent teeth; subsequent treatment of adjacent teeth results in the same pattern of phantom migration. The reader is advised to recall the discussion of neuropathic pain and the origins of perception, distinct from sensation, in the introductory sections of this chapter.

Etiology

The etiology of phantom pain in general and certainly phantom tooth pain in particular is not known. However, many of the features of phantom tooth pain parallel the experiences of limb amputees. Phantom pain in general is a well recognized though poorly understood phenomenon that affects 80% of limb amputees during the immediate postoperative and healing period and remains permanently to some lesser degree for the majority of patients. Several theories exist that only partly explain some of the phantom pain phenomena, but no unifying theory exists that describes all features. These theories focus on pathologic neuroplasticity in the CNS as a result of intense nociceptive afferent activity and neural injury following amputation. The sympathetic nervous system is believed to play a role in several features of phantom pain (see Chapter 33).

Pulp amputation, more than tooth extraction, has been shown to result in peripheral neuropathology (neuroma formation) as well as CNS neuropathology (degeneration of local and projection neurons in the CNS). Ample experimental evidence exists to demonstrate that the sensory map of the periphery can be immediately and permanently altered following tissue and nerve injury. This central neuroplasticity is the physiologic substrate by which one can understand how sensations and pain can “move” or spread from one area to another. Consider the common experience of the genuine perception of a swollen lip following anterior maxillary anesthesia. While the perception of a swollen lip is very real, certainly the lip is not swollen; that is, there is no physical correlate of swelling. However, the local anesthetic immediately altered the relative amount of neural activity and led instantly to a change in perception of body size and shape. In the same way, nerve injury can lead to altered nerve activity that results in phantom pain and dysmorphic perceptions that have a very real physiologic, though not physical, basis.

Perhaps the most provocative theory to explain phantom pain sensations is Melzack’s neuromatrix theory. This theory proposes a genetically determined but experience-dependent neurosignature, a person’s representation of self somewhere in the brain, which once established, exists to some degree independent of the continued existence of various body parts. This neurosignature can be accessed to contribute to awareness of body size and shape by any number of neural processes, including those that are independent of any peripheral input. Thus, injury to the nervous system by removal of a body part does not eliminate awareness of that body part, rather it changes whatever neurophysiologic dynamics maintained that awareness in some healthy and accurate form. The undeniable perception of altered body size or shape, or pain from a body part that does not exist, therefore, becomes a product of altered CNS activity and how that activity relates to the neurosignature of an individual. Considerable psychophysical and physiologic experimentation is currently underway to explore this theory in more detail. There is little doubt that psychological factors contribute to phantom sensations, but little evidence to suggest that the phantom is a result of psychological illness.

Diagnosis

Phantom pain, although likely initiated by peripheral injurious events (amputation), is certainly predominantly maintained by CNS processes. The diagnosis of PTP is a clinical diagnosis based on the history and examination. The patient with PTP complains of persistent deep, dull, aching pain in a denervated tooth or at the site of an extracted tooth; not uncommonly the patient may have difficulty identifying the precise tooth that is painful. There may be occasional periods of sharp pain. The phantom may emerge days, weeks, months, and even years after the initial injury, making identification of the antecedent injury potentially difficult. There are no associated radiographic abnormalities, and pain is not worsened by mechanical or thermal stimulation. The possibility for local odontogenic pain should be considered and careful examination performed to be sure no somatic source of pain exists (fractured tooth, failed root canal therapy). However, the clinician must be cautious not to assume an odontogenic source when there is no evidence to support the diagnosis, and should not initiate treatment based on that assumption. Although potentially frustrating to both patient and doctor, initiating inappropriate treatment based on an unsupported diagnosis will not improve the condition and is more likely to worsen it. As difficult as it may be, offering no treatment is preferable to inappropriate treatment.

Treatment

Treatment of PTP is challenging and generally is based on local (injection) and oral medications, always combined with cognitive therapy and psychological counseling. The patient must be reassured that the pain is not imagined and does not represent an undiagnosed serious disorder (ie, cancer). The patient must be educated
about the nature of the problem so he or she comprehends how the nervous system itself can lead to such painful perceptions.

Medical therapy includes the use of neuropathic pain analgesics, such as tricyclic antidepressant medications (amitriptyline, nortriptyline) and GABA agonists, such as baclofen and clonazepam. Some patients require fixed daily doses of oral narcotic, though this should only be pursued by clinicians familiar with the addictive and medical complications of chronic narcotic use. A trial of the anticonvulsant carbamazepine may be appropriate if other treatment fails. Although it is unlikely to relieve PTP, if the patient does experience relief, one should consider the possibility that the patient suffers from trigeminal neuralgia. A relatively new anticonvulsant medication, gabapentin, may provide relief for PTP, as it has been found to be effective in other neuropathic deafferentation pain disorders, though no study has examined its use in PTP.

Some authorities recommend the use of repeated injection with long-acting local anesthetic (without epinephrine) combined with low-dose corticosteroid (dexamethasone); both have been shown to reduce neuronal excitability at sites of nerve injury. The success of injection therapy depends on selection of the correct site for injection. A careful history and examination are essential to precisely identify the location of the phantom pain or pains. In addition to sites at the teeth, others are at the terminal points of the trigeminal divisions (ie, supraorbital, infraorbital, nasolabial, mental). Efficacy of repeated injection for PTP awaits well-designed, prospective clinical trial.

**Sympathetically maintained pain**

**Clinical features**
The role of the sympathetic nervous system in the initiation or maintenance of chronic neuropathic pain has been a topic of considerable debate and some confusion; its role in orofacial neuropathic pain is understood even less. Adding to the confusion, it has been known by other terms, such as causalgia and reflex sympathetic dystrophy. Sympathetically maintained pain (SMP) may be an independent pain disorder, or a contributing pathologic process to other orofacial neuropathic pain, most notably nerve injury and phantom tooth pain. When SMP is a major component of a neuropathic pain, the features include constant aching and burning pain with periods of exacerbation. The pain may at times be accompanied by other signs of sympathetic dysregulation in the affected region, such as altered local skin temperature, excessive sweating, and trophic changes, although none of these signs is essential in SMP. In all cases where SMP is involved, there is a history of prior injury. The pain is worsened during periods of physiologic or psychological stress and often following injection of a solution containing epinephrine into the painful region.

**Etiology**
Although a single unifying, accepted theory for SMP does not exist, several well-developed models provide a theoretic basis for the disorder. In general, it is proposed that following injury, sympathetic-sensory coupling occurs in which nociceptors upregulate α-adrenergic receptors and respond to norepinephrine released from sympathetic terminals in the injured region. The sympathetically generated nociceptor activity produces a dynamically maintained state of CNS sensitization and hyperexcitability such that activity in low-threshold mechanoreceptors, which normally is not painful, results in allodynia and mechanical hyperalgesia. Regional sympathetic blockade interrupts the sympathetic-sensory coupling and resets the CNS neurons to a desensitized state, relieving spontaneous pain and allodynia. Injection of epinephrine into the affected region worsens or rekindles the pain.

**Diagnosis**
The features of SMP are not unique to the condition and are seen in other nonparoxysmal neuropathic pain conditions: constant burning, aching, or cramping pain, allodynia, and hyperalgesia. However, by definition SMP is abolished when sympathetic activity to the affected region is blocked. Thus, the diagnostic test for SMP requires sympathetic blockade by one of two means: local anesthetic blockade of the stellate ganglion (performed by an anesthesiologist) or intravenous administration of phentolamine, an α-adrenergic antagonist. Contrary to early suggestion that signs of autonomic dysfunction must be present for a diagnosis of SMP, it is now recognized that such signs are not required. That is, the signs of sympathetic dysregulation (altered local skin temperature, excessive sweating, and trophic changes) are dissociated from the pain condition. If sympathetic blockade is achieved yet there is no reduction in pain, then the condition is a sympathetically independent pain (SIP).

**Treatment**
Treatment of SMP requires chronic blockade of sympathetic activity in the affected region. This is achieved by repeat stellate ganglion blockade or sympathectomy. Several reports describe the use of clonidine, available in a slow-release patch, for SMP. Clonidine is an agonist for the presynaptic adrenergic autoreceptor, which then reduces the presynaptic release of norepinephrine. Sympathetic blockade can result in postural hypotension and bradycardia.