24

Phantom Limb Pain

Lee-Ann Rhodes

OVERVIEW

Phantom limb pain can be a devastating consequence of an amputation. It is often a chronic, disabling condition. This chapter reviews the etiology, pathophysiology, prevention, and treatment of phantom limb pain and discusses known risk factors for this condition. Even though many physicians have been frustrated by the inability to control phantom limb pain, promising new therapies are on the horizon.

Malawer Chapter 24 22/02/2001 08:49 Page 370

CLINICAL PRESENTATION

> Nearly every man who loses a limb carries about with him a constant or inconstant phantom of the missing member, a sensory ghost of that much of himself. The sensation of the presence of the part removed exists in many persons as soon as they come from under the influence of the anaesthetic used at the time of the amputation, but in others it only arises after they cease to suffer pain, rarely delayed beyond three weeks. (S. Weir Mitchell[1])

It has been more than a century since Mitchell published his detailed observations about Civil War amputees. Mitchell distinguished several categories of post-amputation phenomena. These categories have become known as phantom limb pain, phantom sensations, stump pain and super-added phantom sensations. Phantom limb pain is a noxious sensation where the limb existed.[2–5] Phantom sensations are nonpainful sensations of the missing limb.[3] Stump pain is pain that is restricted to the amputated site.[4] Super-added phantom sensation describes the sensation of an object, such as a wrist watch or ring, attached to the phantom limb.[4]

Most people with phantom limb pain experience more than one type of pain. Sherman[6] distinguished three major types of pain: lacinating, cramping, and burning. Other types of pain may be sharp; pins-and-needles sensations, itching, pinching, stinging, aching, crushing, twisting, and grinding.[3] The pain typically occurs in the distal region of the phantom limb.[7] The distribution of the pain rarely follows the path of the severed nerve.[2] The pain is often constant and many amputees report having intermittent pain exacerbation.

Patients may report that the phantom limb is in an awkward position, or that it feels as if it were moving either spontaneously or voluntarily.[6,8] The phantom limb may feel so real that an amputee may attempt to reach for objects with the phantom hand or try to step with the phantom foot.[9] In addition, most amputees experience a sense of the length and volume of the missing limb.[8]

The phantom limb may develop a phenomenon called telescoping.[4] This is most often seen in those with painless phantom limbs, and usually occurs within the first year after amputation. As telescoping occurs, the middle portion of the phantom limb is perceived to be shortened while the most highly innervated area, such as a hand or foot, feels as though it is attached close to or directly on the stump.[10] Telescoping occurs more often in the upper than in the lower extremity. With time, amputees may experience the sensation of a markedly shortened phantom limb. The last sensations to disappear are those that have the highest representation in the cortex, such as the index finger, thumb, and great toe.[3]

The existence of the phantom limb may be strengthened by sensations that resemble feelings in the limb that existed prior to the amputation.[11] This phenomenon is termed somatosensory memory[12,13] and may include pains from injury to soft tissues, bones, or joints or other pains that were experienced prior to the amputation.[14,15] For example, pain may be continued from a foot ulceration that was present in the limb prior to amputation.[11] In a further exploration of this concept, Katz and Melzack[14] found 57% of patients who had an amputation as a result of ischemic vascular disease or trauma reported that pain in the phantom limb was similar in location and quality to that experienced in the limb itself prior to amputation; this rate was only 12.5% in patients who had undergone amputation because of a malignancy.

EPIDEMIOLOGY

Phantom limb pain was once thought to be quite rare; most likely because of the patients' reluctance to mention the pain because of fear of ridicule.[3] Many reports have been published regarding the incidence of phantom pain.[16–19] In a survey of 590 veteran amputees, 55% reported phantom pain and 56% reported stump pain.[16] Sherman[6] found that 70% of amputees reported phantom limb pain within the first 2 years following amputation. Up to 88% of patients undergoing hip disarticulation or hemipelvectomy suffer from phantom limb pain.[18] This supports Roth and Sugarbaker's[19] finding that the higher the level of lower extremity amputation, the greater the incidence of moderate to severe pain.

Phantom limb pain occurs soon after amputation and can be long-lasting.[20] Jensen *et al.*[10] found that phantom limb pain occurred within 8 days after amputation in 72% of adult patients. Nikolajsen *et al.*[15] observed that the incidence of phantom pain did not decrease 6 months following amputation, although there was a decrease in the duration of their intermittent pain exacerbations. In 3–10% of amputees the pain is chronic and severe.[16]

Although many children experience phantom sensations, the incidence of phantom limb pain is lower in the pediatric population than in adults.[21] In a retrospective study of 75 pediatric patients, 48% of those with amputations necessitated by cancer and 12% of those who had traumatic amputations reported phantom limb pain.[22] Melzack *et al.*[23] studied a group of pediatric patients who had either a congenital limb deficiency or an amputation before the age of 6 years. Phantom limb sensations were present in 20% of

Malawer Chapter 24 22/02/2001 08:49 Page 371

congenitally limb-deficient subjects and in 50% of those who had undergone amputations before the age of 6. The presence of pain was 20% in the congenital limb-deficient group compared to 42% in the young amputees. Some of the differences between the adults and children may be attributed to under-reporting of pediatric pain.[21] A pediatric study surveying children age 5–19 years who had had an amputation within the previous 10 years found 92% reported pain, although this was reflected in only 50% of the patients' medical records.[21]

In the Melzack *et al*. study,[23] 42% of pediatric amputees developed phantom sensation with a mean onset of 2.3 years. Thirty-five percent of children have resolution of their phantom pain within 10 years of their amputation.[21] Sixty-seven percent of pediatric patients also had a decrease in their phantom sensations, while 14% actually were found to have an increase in their phantom sensations, over a 10-year period.[21]

ETIOLOGY

Preamputation pain is a risk factor in the development of phantom pain following amputation.[10] Even pain that had been experienced in the limb months or years before amputation can be re-experienced as phantom pain.

Nikolajsen *et al*.[15] found that a preamputation pain score greater than 20 mm on the visual analogue scale was associated with an increased risk of phantom pain, but the duration of preamputation pain did not appear to be related to the intensity of phantom pain. The visual analog scale is a 100 mm line with no pain located to the left (0 mm) and worst pain imaginable being to the right (100 mm).[15] Although the incidence of mental illness in patients who develop phantom limb pain is no greater than in those who do not, stress, anxiety, dysphoric mood, and emotional triggers may contribute to the persistence or exacerbation of phantom pain.[6,24–26]

Another factor that may be associated with phantom pain is chemotherapy, especially those agents known to cause peripheral neurotoxicity.[22,27] In a study of pediatric amputees the incidence of phantom limb pain was 74% in patients who had received chemotherapy (either vincristine or cisplatin) prior to amputation. This was reduced to 44% in patients who began chemotherapy after their limb surgery, although all four patients in the postamputation chemotherapy group developed pain within 72 h of the chemotherapy.[22] Phantom limb pain developed in only 12% of patients who never received chemotherapy.[22] It remains unclear whether or not this is also true in adult amputees who have received these chemotherapy agents.

Reappearance of quiescent phantom pain has been reported during spinal anesthesia[28,29] and epidural anesthesia with local anesthetics.[5,30] The pain begins as the block recedes.[31] Although the incidence of rekindling phantom limb pain during spinal anesthesia is quite low (about 5%), it can be severe and difficult to treat.[32–34] Phantom limb pain may also be exacerbated by metastatic disease[3,35] or tumor recurrence.[36] There is a case report of exacerbation of phantom limb pain following magnetic resonance imaging.[37]

PATHOPHYSIOLOGY

It is now widely accepted that phantom limb pain is the result of complex interactions between the peripheral and central nervous systems. At the time of amputation, severing of the peripheral nerves disrupts normal afferent nerve input into the spinal cord. This process, often referred to as deafferentation, results in the degeneration of the distal portion of the peripheral nerves; the proximal portion, however, survives.[7,38]

Subsequently, abnormal discharges develop in the sprouts, known as neuromas, of the regenerating proximal nerves.[39,40] These ectopic abnormal discharges are the result of increased excitability in the sprout, which occurs because of the accumulation of transported chemical mediators. These mediators accumulate in the neuroma following anterograde axoplasmic transport from the cell body to its periphery.[7] Increased firing occurs in the neuroma as it becomes hypersensitive to mechanical, chemical, and metabolic changes.[7]

Peripheral mechanisms do not totally explain the phenomenon of phantom limb pain because conduction blockade of the peripheral nerves usually does not eliminate it.[40] In addition, even if the ectopic discharges resolve spontaneously, surgically, or as a result of pharmacotherapy, phantom limb pain usually persists.[7] This may be because abnormal c-fiber afferent activity, that starts after the amputation of the peripheral nerve leads to changes in the spinal cord itself.[8] Reorganization occurs in the receptive fields of the spinal cord. New synaptic connections form from the axonal sprouting of the proximal section of the amputated peripheral nerve. In areas of the spinal cord that are not responsible for the transmission of pain, some axons that previously terminated begin to sprout into lamina II of the dorsal horn. This lamina is the region that is typically involved in the transmission of painful nociceptive afferent inputs.[7] The dorsal horn of the spinal cord also starts exhibiting central hyperexcitability, as demonstrated by an increased rate of

Malawer Chapter 24 22/02/2001 08:49 Page 372

firing. This process, referred to as the wind-up phenomenon, is mediated by substance P, tachykinins, and neurokinin A's action at the *N*-methyl-D-aspartate (NMDA) receptor, with concomitant up-regulation of the receptors.[7,8] At the same time that the excitability of the dorsal horn of the spinal cord occurs, there is a decrease in the normal inhibitory interneuron activity.[38,40] This interplay leads to the increased transmission of pain signals.

Changes occur not only in the peripheral nervous system and spinal cord but also in the cerebral cortex. It is hypothesized that amputees retain neural activity and function of the thalamic representation of the amputated limb. Evidence in support of this theory has been found during functional stereotactic mapping; microstimulation of certain areas of the ventrocaudal thalamus in amputees produces painful sensations in the phantom limb.[41] In addition, the representation in the thalamus of the stump area increases in some amputees.

This is consistent with the findings of animal studies in which there is enlargement of somatotopically adjacent areas into the deafferentiated regions.[41] This cortical reorganization partly explains some instances in which afferent nociceptive stimulation of neurons within the stump or surrounding areas can produce sensations in the missing limb. This occurs because the region of the cortex that was once responsible for receiving input from the amputated limb is now processing information from the stump and referring the sensation to the phantom limb.[42–44]

The amount of cortical reorganization appears to be directly proportional to the degree of pain.[43] When some amputees experience a reduction of phantom limb pain with local anesthetic conduction blockade (e.g. spinal anesthesia used during surgery), they also experience a temporary reduction in the amount of cortical reorganization in the somatosensory cortex.[45]

In addition to the peripheral and central mechanisms involved in the pathophysiology of phantom pain, Melzack[11,46,47] has described a neuromatrix responsible for phantom limb pain. This matrix is a large, widespread network of neurons that consists of loops between the thalamus and cortex and between the cortex and limbic system.[46] Melzack proposes that there is a genetically determined central representation of the body image that interacts with cognitive and somatosensory memories of the limb and that it is unique to each person. It is modified by the individual's sensory inputs and gives each person a neurosignature, which is a continuous outflow from the neuromatrix to certain brain areas referred to as the sentient neural hub. This hub converts the flow of neurosignatures into the flow of awareness, resulting in the sensations experienced by the amputee.[46] The concept of the neuromatrix allows for contributions of both age-dependent and age-independent experiences of phantom pain and possibly accounts for the lower incidence of phantom limb pain in the pediatric population.[46]

An extension of the neuromatrix theory is that of the phantom limb open-circuit. When an extremity is amputated, the return signal from that limb disappears while the outgoing signal from the neuromatrix remains.[48] This alteration in signals may be responsible for the perception of phantom limb pain. On the basis of this tenet, phantom limb pain may be decreased by either eliminating the outgoing signal from the neuromatrix or by creating a normal return signal via electrical stimulation.[48]

Canavero[49] opposes Melzack's neuromatrix theory of phantom pain on the basis of evidence that a focal brain lesion involving the parietal cortex, thalamus, or corticothalamocortical fibers contralateral to the amputated limb can relieve phantom pain. Melzack contends that the neuromatrix is widespread and therefore not amenable to lesioning. Canavero[49] hypothesizes that prior surgical techniques were inadequate and may some day be used to treat phantom pain. Future work will focus on the selective interruption by bilateral stereotactic lesioning of a local reverberatory loop that sustains phantom limb pain between the sensoricortical area and the thalamus.

PREVENTION

The establishment of analgesia prior to surgical incision (pre-emptive analgesia)[50] may help control postoperative pain by preventing the transmission of noxious afferent input from the periphery to the spinal cord.[51] Otherwise, a prolonged state of central neural sensitization and hyperexcitability could occur that would amplify future input from the amputated site.[52] Epidural and epineural analgesia, given peri-operatively and postoperatively, have revolutionized the ability to manage pain. With these techniques the need for postoperative opioids, as well as their associated side effects, has decreased. Until recently, epidural analgesia was thought not only to optimally manage postoperative pain following an amputation but also to decrease the incidence of phantom limb pain.[53–55] The validity of these studies, however, is questionable because of small sample sizes and insufficient randomization.[56] A recent randomized, double-blind, placebo-controlled study by Nikolajsen *et al.*[56] found that epidural blockade with bupivacaine and morphine did not prevent phantom or stump pain. In this study, epidural analgesia was started at least 15 h

Malawer Chapter 24 22/02/2001 08:49 Page 373

prior to amputation and continued for a minimum of 2 days. The incidence of phantom limb pain and stump pain was the same in the control and epidural groups at 1 week, 3 months, 6 months, and 12 months after the amputation.[56]

Epidural clonidine is now being administered for neuropathic pain. In a prospective, controlled study, 13 patients received epidural infusions containing bupivacaine 75 mg, clonidine 150 μg, and morphine 5 mg in 60 ml of normal saline. The infusion of 1–4 ml/h was initiated 24–48 h preoperatively and continued for at least 3 days. The control group received IV opioid patient-controlled analgesia. The incidence of phantom limb pain was 8% in the epidural group compared to 73% in the control group.

Side-effects of the epidural infusion were temporary urinary retention and bowel incontinence.[57] Before any conclusions can be drawn regarding the prevention of phantom limb pain by the addition of clonidine to the epidural bupivacaine and morphine, a larger study, done in a manner similar to that of Nikolajsen *et al.*[56] is needed.

Postamputation analgesia and prevention of lower extremity phantom limb pain have been investigated using infusions of local anesthetic placed into a nerve sheath via a catheter at the time of amputation.[58,59] Although regional anesthetic techniques offer many advantages of pain control during the perioperative and postoperative periods, the results of several studies are conflicting. Fisher and Meller[60] conducted a pilot study of 11 patients undergoing an above- or below-knee amputation with a continuous perineural infusion of 0.25% bupivacaine at 10 ml/h into the sciatic or posterior tibial nerve sheath. The infusion continued for 3 days. Postoperative opioid requirements were significantly lower compared with those of a retrospective control group, given parenteral opioids. None of the patients who received the peripheral nerve infusions developed phantom limb pain during the 12 months of follow-up.[60] Similar findings were reported by Malawer *et al.*[59] in a study in which local anesthetic was administered directly into the peripheral nerve sheaths following an amputation (Figure 24.1). When compared with historical controls there was an 80% reduction in narcotic requirement for the 72 h following surgery.[59]

Pinzur *et al.*[61] conducted a randomized controlled study in which a local anesthetic was infused adjacent to the transected nerve but not within the nerve sheath. A sciatic nerve catheter was used for transfemoral amputations, while posterior tibial nerve catheters were used for transtibial amputations. All amputations were done because of ischemic changes secondary to peripheral vascular disease. Bupivacaine 0.5% at 1 ml/h was used for the local anesthetic infusion. The control group studied received opioids only. In the first two postoperative days, morphine use was lower in the infusion group than in the control group. By the third postoperative day no statistical significance in opioid requirements was present between the two groups. At 3 and 6 months after the amputation there was no difference in the incidence of phantom limb pain between the infusion and control group.[61] It is possible that some of the differences may be attributed to the placement of the catheter adjacent to the nerve ending instead of threading it up the sheath, combined with the low volume (1 ml versus 4–10 ml/h) of local anesthetic given hourly in the Pinzur study compared with that given by Fisher and Meller.[62]

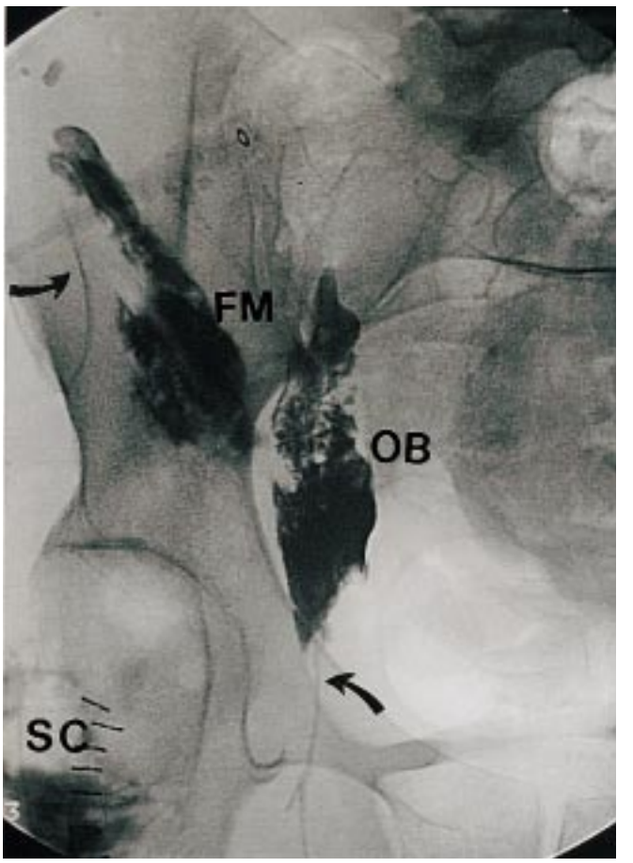

Figure 24.1

Malawer Chapter 24 22/02/2001 08:49 Page 374

A retrospective, unblinded study of patients who had undergone lower extremity amputations compared the incidence of phantom limb pain in patients receiving a continuous infusion of bupivacaine 0.5% with those receiving only opioids. Bupivacaine at 2–6 ml/h was infused via a catheter into the sciatic or posterior tibial nerve sheath. The catheter was placed under direct supervision during surgery. In the infusion group a bolus of 10–20 ml of 0.5% bupivacaine was given shortly before the end of surgery. The catheters were maintained for 3–7 days. Postoperative opioid requirements and the incidence of phantom limb pain at 6 months were not significantly different between the two groups.[63] Two limitations of this study were the use of a heterogeneous group of patients having amputations for a variety of conditions, and variations in the extent of preoperative pain. The use of a single-nerve catheter, instead of multiple catheters that included both the femoral and sciatic nerve, may have contributed to the failure of bupivacaine to produce superior results.[63]

TREATMENT

Although numerous modalities exist for the treatment of neuropathic pain, many have shown only limited success (Table 24.1). Many of the studies of the effectiveness of pharmacotherapeutic agents have been done with small groups of patients and with no long-term follow-up.[64]

Antidepressants, particularly those from the tricyclic group, and anticonvulsants are frequently administered for the treatment of neuropathic pain.[8,43] However, double-blinded studies are needed to confirm their effectiveness in relieving phantom pain. Case reports show improvement in phantom limb pain using clonazepam[65] or fluoxetine, even in the absence of a coexisting affective disorder.[66] Beta-blockers have also been used for phantom limb pain;[8,67] their efficacy is unclear.[3]

Sherman[64] has found that burning and cramping components of phantom limb pain may each respond to different agents. Burning pain may be decreased by increasing the blood flow to the stump via nitroglycerine ointment or nifedipine, while muscle relaxants may relieve cramping pain.[64]

Infusions of drugs may also decrease phantom limb pain. MacFarlane *et al.*[7] found that five daily doses of IV lidocaine (3 mg/kg) given over 30 min for up to 4 days may produce prolonged relief. The oral antiarrhythmic agent, mexilitine, can be initiated if pain returns following an IV lidocaine infusion.[7] A 1 mg/kg bolus of IV lidocaine has been given to treat chronic phantom pain and severe phantom pain flare-ups.[33]

After several case reports revealed decreased phantom limb pain with calcitonin infusions, Jaeger and Maier[68] conducted a double-blind study with 200 IU of salmon calcitonin administered IV to patients with phantom pain. A second infusion was given to several patients who continued to experience pain. At 1-year follow-up 62% of amputees receiving calcitonin had greater than 75% pain relief. Relief extended to 2 years in 58% of the patients.[68]

A great deal of excitement has been generated regarding the use of NMDA receptor antagonists in the treatment of neuropathic pain. The blockade of the NMDA receptor may reduce central hyperexcitability. In a randomized, double-blinded study of patients with persistent phantom limb pain, the NMDA receptor antagonist, IV ketamine, was given via a 0.1 mg/kg bolus over 5 min followed by an infusion of 7 μg/kg/min of ketamine for up to 45 min. During the infusion, and in some cases up to 3 days thereafter, ketamine relieved pain in the stump and the phantom limb to the same extent.[39] In a case report, ketamine produced pain relief when infused at 0.12 mg/kg/h in a

Table 24.1 Reported treatments used for phantom limb and stump pain

Medical interventions	*Psychological interventions*	*Physical modalities*	*Invasive modalities*
Opioids, antidepressants, anticonvulsants, sodium channel blockers, NMDA receptor antagonists, calcitonin	Relaxation, imagery, hypnosis, behavioral therapy, psychotherapy, biofeedback	Acupuncture, stump desensitizing, TENS to contalateral limb, auricular TENS, percussion of stump, prosthesis adjustment, heat or cold to stump, stump massage, stump ultrasound, physical therapy	Revisions of the stump, neuroma resection, sympathectomy, dorsal rhizotomy, dorsal root entry zone lesioning, dorsal cordotomy, anterolateral cordotomy, spinal cord stimulation, thalamic stimulation, stump neuroma injections, sympathetic blockade, intrathecal infusions, epidural infusions

Malawer Chapter 24 22/02/2001 08:49 Page 375

pediatric amputee who developed severe phantom pain following chemotherapy.[27]

Long-term opioid therapy can be used in the treatment of phantom limb pain; however, neuropathic pain may be less responsive to opioids than nociceptive pain and requires higher doses.[69] This may be in part attributed to a reduction in the number of opioid receptors expressed on c-fiber afferents following peripheral nerve damage.[70] The total amount of opioid required to achieve analgesia may be less when it is combined with other agents, such as the tricyclic antidepressants or anticonvulsants, that are used in pain modulation.

While ketamine has been shown to play a role in reducing neuropathic pain, its use may be limited by central nervous system side-effects such as insobriety.[39] Recently, a noncompetitive NMDA receptor antagonist, amantadine, was found to reduce surgical neuropathic pain in cancer patients.[71] In a placebo-controlled randomized study, 200 mg of amantadine was infused over 3 h. Fifteen patients participated in this study. The types of neuropathic pain they had were associated with post-thoracotomy pain syndrome, post-mastectomy pain syndrome, ilioinguinal neuropathy, femoral neuropathy, and scar neuroma. Pain decreased by 85% following the infusion and continued for up to 48 h.[71] The ability of IV amantadine to control phantom limb pain and the role of oral amantadine are unknown, and should be subjected to further evaluation.

Novel treatments that may have an impact on reducing phantom limb pain include cyclo-oxygenase inhibitors,[72] nitric oxide synthesis inhibitors,[73] and axoplasmic transport modifiers.[74] Drugs that would prevent central sensitization are also being investigated.[75]

Since no single form of treatment has been shown to consistently reduce phantom limb pain, an interdisciplinary approach may yield the best outcome. Physical therapy can help improve strength, flexibility, and balance in amputees. Refitting the prosthesis may result in a decrease in stump and phantom pain, although the severity of phantom pain does not appear to correlate with the amount of prosthesis use.[19] Applying transcutaneous electrical nerve stimulation (TENS) to the contralateral limb may decrease phantom limb pain; however, exacerbation of pain has been documented from TENS use on the stump and should be avoided.[4,76,77]

Katz and Melzack[77] reported painful throbbing and pressure of phantom limbs are reduced by low-frequency (4 Hz), high-intensity (10–30 V) auricular TENS.[77] The mechanism proposed for pain reduction is secondary to activation of brainstem structures that exert an inhibitory control over nociceptive neurons in the spinal cord dorsal horn.[8] Long-term follow-up was not done.

Other forms of therapy that have been described include acupuncture, guided imagery, hypnosis, and relaxation techniques.[43,78] Sherman[64] found that patients with the burning component of phantom pain may experience a reduction in pain by temperature biofeedback or multiple sympathetic blockade, while cramping phantom pain may be decreased by biofeedback.

Intrathecal injections, with such agents as fentanyl, have been investigated for use in relieving phantom limb pain.[79] The partial opioid antagonist, buprenorphine, given intrathecally, has been shown to decrease baseline pain in several patients. This decrease is prolonged by switching to buprenorphine suppositories.[80] The selective neuronal voltage-sensitive calcium channel blocker, SNX-11, acts by blocking neurotransmitter release at the primary afferent nerve terminals. Continuous intrathecal administration of this drug reduced intractable phantom limb pain.[81]

Phantom limb pain generally does not respond to surgical intervention.[3] Stump neuromas develop at the site of the severed end of peripheral nerves and may trigger phantom pain.[40] Surgical management may involve implanting the proximal end of the cut nerve into an adjacent bone or a nearby site.[7] While this may decrease stump pain, it usually does not permanently relieve phantom pain.[4] Neuroablative neurosurgical procedures are now rarely performed.

Anterolateral cordotomy provides only short-term relief, since the spinal cord contains a network of interconnecting fibers that will eventually resume the functions originally performed by the severed tract.[82] Dorsal root entry zone (DREZ) lesioning can selectively abolish phantom limb, but not stump, pain.[82] Saris *et al*.[82] reported that 36% of such patients had pain relief with a follow-up period ranging from 6 months to 4 years. They also found that nine out of 22 patients developed minor but chronic neurologic deficits.[82] The results of DREZ lesioning are more promising in patients who undergo traumatic amputation than in oncology patients.[83]

Spinal cord stimulation has also been used for phantom limb pain.[84] Seigfried *et al*.[85] reported that 51% of patients with implanted spinal cord stimulators had a 50% or more decrease in pain, while 18% obtained a 25–50% reduction in pain. Long-term follow-up is needed to determine whether the initial relief is sustained over time.

Finally, intracranial neurostimulation has been used for phantom limb pain. Stimulation of the parvocellular part of the nucleus ventralis posterolateralis of the thalamus has led to a decrease in phantom limb pain;[86]

Malawer Chapter 24 22/02/2001 08:49 Page 376

however, in most cases pain control has not been permanent.[3]

CONCLUSION

An interdisciplinary approach to pain management and rehabilitation can provide amputees with the best chance of a pain-free outcome.[8] Members of the team may include representatives from medical and surgical oncology, rehabilitation medicine, pain medicine, behavioral medicine, and nursing. Preoperative patient education programs are also essential.[87] Psychological support and reassurance can alleviate anxiety that often follows amputation. Amputees need to be aware of their postoperative pain management options and to understand that their pain will be aggressively managed. It is important that these options also be addressed in the preoperative conference. Rehabilitation is initiated prior to the patient's discharge. In many amputees pain is the major limiting factor in rehabilitation. To achieve a functional lifestyle as soon as possible, it is mandatory that we use every available means to control pain.[40]

If persistent pain develops, a comprehensive evaluation is necessary. The impact of the pain on the patient's psychosocial and physical functioning is an integral part of this assessment. A treatment plan based on the contributions of different specialists of the interdisciplinary team can then be formulated.

References

1. Mitchell SW. Injuries of Nerves and their Consequences. Philadelphia: J.B. Lippincott; 1872.
2. Carlen PL, Wall PD, Nadvorna H, Steinbach T. Phantom limbs and related phenomena in recent traumatic amputations. Neurology. 1978;28:211–17.
3. Raj PP. Practical Management of Pain. Mosby Year Book, 1992.
4. Wesolowski JA, Lema MJ. Phantom limb pain. Reg Anesth. 1993;18:121–7.
5. Katz J, Melzack R. Pain memories in phantom limbs: review and clinical observations. Pain. 1990;43: 319–36.
6. Sherman RA. Stump and phantom limb pain. Neurol Clin. 1989;7:249–64.
7. MacFarlane BV, Wright A, O'Callaghan J, Bensen HA. Chronic neuropathic pain and its control by drugs. Pharmacol Ther. 1997;75:1–19.
8. Jensen TS, Rasmussen P. Phantom pain and related phenomena after amputation. Wall PD, Melzack R, editors. Textbook of Pain, 2nd edn. Edinburgh: Churchill Livingstone; 1989:000–00.
9. Melzack R, Wall PD. The Challenge of Pain. London: Penguin; 1985.
10. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Phantom limb, phantom pain and stump pain in amputees during the first six months following amputation. Pain. 1983;17: 243–56.
11. Melzack R. Phantom limbs. Sci Am. 1992;266:120–6.
12. Baron R, Maier C. Phantom limb pain: are cutaneous nociceptors and spino-thalamic neurons involved in the signaling and maintenance of spontaneous and touch-evoked pain Pain. 1995;60:223–8.
13. Katz J. Psychophysiological contributions to phantom limbs. Can J Psychiatry. 1992;37:282–98.
14. Katz J, Melzack R. Pain memories in phantom limbs: review and clinical observations. Pain. 1990;43:319–36.
15. Nikolajsen L, Ilkjaer S, Kroner K, Christensen JH, Jensen TS. The influence of preamputation pain on postamputation stump and phantom pain. Pain. 1997;72:393–405.
16. Wartan SW, Hamann W, Wedley JR, McColl I. Phantom pain and sensation among British veteran amputees. Br J Anaesth. 1997;78:652–9.
17. Katz J. Prevention of phantom-limb pain by regional anesthesia. Lancet. 1997;349:519–20.
18. Postone N. Phantom limb pain: a review. Int J Psychiatry Med. 1987;17:57–70.
19. Roth YF, Sugarbaker PK. Pains and sensations after amputation: Character and clinical significance. Arch Phys Med Rehabil. 1980;61:490.
20. Melzack R. Phantom limb pain: implications for treatment of pathologic pain. Anesthesiology. 1971;35: 409–19.
21. Krane EJ, Heller LB. The prevalence of phantom sensation and pain in pediatric amputees. J Pain Symptom Manage. 1995;10:21–9.
22. Smith J, Thompson JM. Phantom limb pain and chemotherapy in pediatric amputees. Mayo Clin Proc. 1995;70:357–64.
23. Melzack R, Israel R, Lacroix R, Schultz G. Phantom limbs in people with congenital limb deficiency or amputation in early childhood. Brain. 1997;120:1603–20.
24. Hill A, Niven CA, Knussen C. Pain memories in phantom limbs: a case study. Pain. 1996;66:381–4.
25. Ewalt JR, Randall GC, Morris H. The phantom limb. Psychosom Med. 1947;9:118–23.
26. Kolb LC. The Painful Phantom. Charles Thomas Press; 1954.
27. Knox DJ, McLeod BJ, Goucke CR. Acute phantom limb pain controlled by ketamine. Anaesth Intens Care. 1995;23:620–2.
28. Alderson JD. Phantom limb pain and spinal anesthesia. Anaesthesia. 1994;49:924.

Malawer Chapter 24 22/02/2001 08:49 Page 377

29. MacKenzie N. Phantom limb pain during spinal anesthesia. Anesthesia. 1983;38:886–7.
30. Uncles R, Glynn CJ, Carrier LES. Regional anesthesia for repeat cesarean section in a patient with phantom limb pain. Anesthesia. 1996;51:69–70.
31. Dureja GP Sandhya. Phantom limb pain during labor. Anesthesia. 1992;47:1053–4.
32. Tessler MJ, Kleiman SJ. Spinal anesthesia for patients with previous lower limb amputations. Anesthesia. 1994;49:441.
33. Lamacraft G. Lignocaine for acute phantom limb pain reactivation by regional anaesthesia. Anaesthesia. 1996; 51:800–1.
34. Fiddler DS, Hindman BJ. Intravenous calcitonin alleviates spinal anesthesia-induced phantom limb pain. Anesthesiology. 1991;74:187–9.
35. Chang VT, Tunkel RS, Pattillo BA, Lachmann EA. Increased phantom limb pain as an initial sympton of spinal-neoplasia. J Pain Symptom Manage. 1997;13:362–4.
36. Roth YF, Sugarbaker PH, Weiss CM, Davidson DD. Increasing phantom limb pain as a symptom of cancer recurrence. Cancer. 1984; 54:373–5.
37. Yuh WT, Fisher DJ, Shields RK, Ehrhardt JC, Shellock FG. Phantom limb pain induced in amputee by strong magnetic fields. J Mag Reson Imag. 1992;2:221–3.
38. Williams AM, Deaton SB. Phantom limb pain: elusive, yet real. Rehab Nursing. 1997;22:73–7.
39. Nikolajsen L, Hansen CL, Nielsen J, Keller J, Arendt-Nielsen L, Jensen TS. The effect of ketamine on phantom pain: a central neuropathic Disorder maintained by peripheral input. Pain. 1996;67:69–77.
40. Weinstein SM. Phantom pain. Oncology. 1994;8:65–70.
41. Davis KD, Kizz ZHT, Luo L, Tasker RR, Lozano AM, Dostrovsky JO. Phantom sensations generated by thalamic microstimulation. Nature. 1998;391:385–7.
42. Kaas JH. Phantoms of the brain. Nature. 1998;391:331–3.
43. Flor H, Elbert T, Knecht S *et al.* Phantom-limb pain as a perceptual correlate of Cortical reorganization following arm amputation. Nature. 1995;375:482–4.
44. Halligan PW, Marshall JC, Wade DT, Davey J, Morrison D. Thumb in cheek; sensory reorganization and perceptual plasticity after limb amputation. Neuro Report. 1993;4: 233–6.
45. Birbaumer N, Lutzenberger W, Montoya P *et al*. Effects of regional anesthesia on phantom limb pain are mirrored in changes in cortical reorganization. J Neurosci. 1997;17: 5503–8.
46. Melzack R. Pain: past, present, and future. Can J Exp Psychiatry. 1993;47:615–29.
47. Melzack R. Phantom limbs and the concept of neuromatrix. Trends Neurosci. 1990;13:88–92.
48. Kingham DJ. On the general theory of neural circuitry. Med Hypoth. 1994;42:291–8.
49. Canavero S. Dynamic reverberation. A unified mechanism for central and phantom pain. Med Hypoth. 1994;42:203–7.
50. Newman P, Fawcett W. Pre-emptive analgesia. Lancet. 1993;342:562.
51. Katz J. Prevention of phantom pain by regional anaesthesia. Lancet. 1997;349:519–20.
52. Katz J. Phantom limb pain. Lancet. 1997;350:1338–9.
53. Bach S, Noreng MF, Tjellden NU. Phantom limb pain in amputees during the first 12 months following limb amputation, after preoperative lumbar epidural blockade. Pain. 1988;33:297–301.
54. Shug SA, Burrell R, Payne J, Tester P. Preemptive epidural analgesia may prevent phantom limb pain. Reg Anesth. 1995;20:256.
55. Katsuly-Liapis I, Georgakis P, Tierry C. Preemptive extradural analgesia reduces the incidence of phantom pain in lower limb amputees. Br J Anesth. 1996;76:125.
56. Nikolajsen L, Ilkjaer S, Christensen JH, Kroner K, Jensen TS. Randomized trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. Lancet. 1997;350:1353–7.
57. Jahangiri M, Jayatunga AP, Bradley JWP, Dark CH. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. Ann R Coll Surg Engl. 1994; 76:324–6.
58. Pavy TJ, Doyle DL. Prevention of phantom limb pain by infusion of local anaesthetic in the sciatic nerve. Anaesth Intens Care. 1996;24:599–600.
59. Malawer MM, Buch R, Khurana JS, Orth MS, Garvey T, Rice L. Postoperative infusional continuous regional analgesia. A technique for relief of postoperative pain following major extremity surgery. Clin Orthop. 1991;266: 227–37.
60. Fisher A, Meller Y. Continuous postoperative regional analgesia by nerve sheath block for amputation surgery a pilot study. Anesth Analg. 1991;72:300–3.
61. Pinzur MS, Garla PGN, Pluth T, Vrbos L. Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. A randomized clinical trial. J Bone Joint Surg Am. 1996;78A:1501–5.
62. Enneking FJ, Morey TE. To the Editor, Correspondence. J Bone Joint Surg Am. 1997;79A:1752–3.
63. Elizaga AM, Smith DG, Sharar SR, Edwards T, Hansen ST. Continuous regional analgesia by intraneural block: effect on postoperative opioid requirements and phantom limb pain following amputation. J Rehab Res Dev. 1994;31: 179–87.
64. Sherman RA. Phantom limb pain mechanism based management. Clin Podiatric Med Surg. 1994;11:85–106
65. Bartusch SL, Sanders BJ, D'Alessio JG, Jernigan JR. Clonazepam for the treatment of lancinating phantom limb pain. Clin J Pain. 1996;12:59–62.
66. Power-Smith P, Turkington D. Fluoxetine in phantom limb pain. Br J Psychiatry. 1993;163:105–6.
67. Iocona RP, Lindford J, Sandyk R. Pain management after lower extremity amputation. Neurosurgery. 1987;20:496–500.
68. Jaeger H, Maier C. Calcitonin in phantom limb pain: a double-blind study. Pain. 1992;48:21–7.
69. Portenoy RK, Foley KM, Inturnsi CE. The nature of opioid responsiveness and its implications for neuropathic pain: new hypothesis derived from studies of opioid infusions. Pain. 1990;43:273–86.
70. Dickerson AH. Where and how do opioids act? In: Gebhart GF, Hammond DL, Jensen TS, editors.

Malawer Chapter 24 22/02/2001 08:49 Page 378

Proceedings of the 7th World Congress on Pain. Progress in Pain Research Management. Seattle: IASP Press; 1991;525–52.
71. Pud D, Eisenberg E, Spitzer S, Adler R, Fried G, Yarnitsky D. The NMDA receptor antagonist amantadine reduces surgical neuropathic pain in cancer patients: a double blind, randomized placebo controlled trial. Pain. 1998; 75:349–54.
72. Brune K. Spinal cord effects of antipyretic analgesics. Drugs. 1994;47:21–7.
73. Malmberg AB, Yakish TL. Spinal nitric oxide synthesis inhibition blocks NMDA induced thermal hyperalgesia and produces antinociception in the formalin test in rats. Pain. 1993;54:291–300.
74. Porubesanski Z, Csillik B. Transganglionic effects of Nocodazole, a new synthetic microtubule inhibitor, upon the histochemical structure of the spinal upper dorsal horn. J Hirnforsch. 1992;33:169–71.
75. Woolf CJ, Chong MS. Preemptive analgesia: treating postoperative pain by preventing the establishment of central sensitization. Anaesth Analg. 1993;77:362–79.
76. Katz J, France C, Melzack R. An association between phantom limb sensations and stump skin conductance during nerve transcutaneous stimulations. Pain. 1989; 36:367–77.
77. Katz J, Melzack R. Auricular transcutaneous electrical nerve stimulation (TENS) reduces phantom limb pain. J Pain Symptom Manage. 1991;6:73–83.
78. Patterson JW. Banishing phantom pain. Nursing. 1994; 24:64.
79. Jacobsen J, Chabal C, Brody MC. Relief of persistent post amputation stump and phantom limb pain with intrathecal fentanyl. Pain. 1989;37:317–22.
80. Omote K, Ohmori H, Kawamata M, Matsumoto M, Namiki A. Intrathecal Buprenorphine in the treatment of phantom limb pain. Anesth Analg. 1995;80:1030–2.
81. Brose WG, Gutlove DP, Luther RR, Bowersox SS, McGuire D. Use of intrathecal SNX-111, a novel, N-type, voltage-sensitive, calcium channel blocker, in the management of intractable brachial plexus avulsion pain. Clin J Pain. 1997;13:256–9.
82. Saris SC, Iacono RP, Nashold BS. Dorsal entry zone lesions for post amputation pain. J Neurosurg. 1985;62:72–6.
83. Nashold BS Jr, Ostdahl RH, Bullitt E, Friedman A, Brophy B. Dorsal root entry zone lesions: a new neurosurgical therapy for deafferentation pain. Bonica JJ, editor. Advances in Pain Research and Treatment. New York: Raven Press; 1983:739–50.
84. van Dongen VCPC, Liem AL. Phantom limb and stump pain and its treatment with spinal cord stimulation. J Rehab Sci. 1995;8:110–4.
85. Seigfried J, Zimmerman M. Phantom and stump pain. Berlin: Springer Verlag; 1981:148–55.
86. Tasker RR, Kizz ZHT. The role of the thalamus in functional neurosurgery. Neurosurg Clin N Am. 1995;6: 73–104.
87. Portenoy RK. The Weinstein article reviewed. Oncology. 1994;8:73–4.