

# Pain after amputation

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## Key points

Three separate phenomena can occur after amputation of a body part – phantom sensation, stump pain and phantom pain.

Phantom limb pain is a common and difficult condition to treat.

There is insufficient evidence to support the routine use of preoperative epidural anaesthesia as a technique to prevent phantom limb pain.

Risk factors for the development of phantom limb pain include persistent stump pain, bilateral and lower limb amputations and pre-amputation pain.

Surgical revision for stump pain is only indicated when localized pathology is identified.

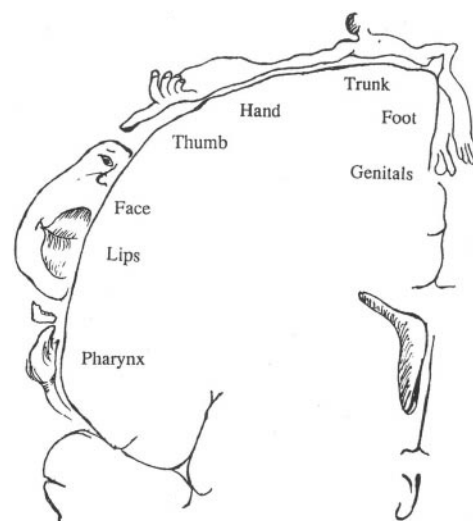
Amputation of a body part, whether as a result of trauma or surgical intervention, is almost always associated with awareness of, and sensations referred to, the missing body part. These sensations were first noted by Ambroise Pare, a French military surgeon in the middle of the 16th century. Mitchel first used the term 'phantom' in 1871 from his observations and medical studies of the American civil war.

Three phenomena occur after amputation – (i) phantom sensation, (ii) stump pain and (iii) phantom pain. While limbs are most commonly involved, the same problems can occur with teeth, breast and rectum.

## Phantom sensation

The term 'phantom sensation' describes any sensation that is experienced in the absent part excluding pain. Its incidence is very high, with virtually all amputees describing phantom limb sensations. A variety of sensations can be felt, including the perception that the missing limb is still present and paraesthesia occurring in the amputated limb. The phenomenon of telescoping occurs when the distal part of the missing limb is felt to recede back towards the stump; forearm amputees often describe that they feel that their amputated hand is attached to their elbow stump. Telescoping probably occurs because of the cortical magnification of the hand, as it is proportionally over-represented on the somatosensory cortex (Fig. 1).

Phantoms appear immediately after amputation in most cases, but their appearance may sometimes be delayed by days or even weeks. These sensations have a variable duration lasting from weeks to years. Phantom limb sensations are rarely a clinical problem, as by definition they are not painful. Careful explanation is needed to allay the patient's fears and to reassure them that these sensations are normal and expected after amputation. This is particularly important in children, who are often frightened by these phenomena.



**Fig. 1** The Penfield 'homunculus'. Reproduced from Ramachandran VS, Hirstein W. The perception of phantom limbs. *Brain* 1998; **121**: 1603–30, by permission of Oxford University Press.

## Stump pain

Stump pain that occurs immediately after amputation is acute nociceptive pain and usually resolves after a few weeks as the wound heals. Infection or wound dehiscence may prolong postoperative pain in some cases. Stump pain can persist for much longer than the initial period of wound healing, lasting months or years, and occurs in 13–71% of cases. This may be secondary to localized pathology or to the development of a neuropathic pain process. It may also occur as a result of peripheral neuropathy (e.g. in those with diabetes).

Persistent stump pain can be very difficult to treat, and management depends on the aetiology; diagnosis is therefore very important. Surgical revision of the stump site is only indicated when localized pathology is identified (e.g. bone spurs, skin lesions, circulatory insufficiency, osteomyelitis or abscess). Liaison with rehabilitation and limb-fitting services is very important. In some cases, simply changing an ill-fitting prosthesis may be all that is required. Where there is no obvious localized pathology, it is best to avoid surgical revision of the stump and treat similarly to phantom limb pain.

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## Phantom pain

The precise incidence of phantom pain is not known. Reported rates vary from 4 to 78%, and recent evidence suggests rates of approximately 50–78%.

### Signs and symptoms

Phantom pain normally occurs within the first week after amputation. However, some studies have reported the development of phantom limb pain months or years after the initial amputation. It can occur for the first time if a patient with a prior lower limb amputation is given a spinal anaesthetic for another procedure. Spinal or epidural anaesthesia can also temporarily exacerbate phantom limb pain in patients with a prior lower limb amputation. Induction of phantom limb pain with regional anaesthesia has been reported in patients who have been symptom-free for as long as 40 years and may occur during the onset or regression of the block. The pathophysiology behind this bizarre phenomenon is not completely understood. A proposed mechanism is loss of segmental afferent input, as a result of spinal or epidural anaesthesia, leading to a decreased input to the brainstem mechanisms normally exerting an inhibitory influence on sensory transmission. The release from this descending inhibition may allow upward transmission of abnormal neuronal activity.

Phantom pain has been described in various terms (*e.g.* shooting, burning, cramping and aching) and is characteristically localized in the distal area of the phantom limb. In some amputees, the pain may be constant but of varying intensity. Others more commonly experience intermittent episodes of high-intensity pain on a daily, weekly or less frequent basis. The duration of symptoms is unpredictable, resolving in months in a few amputees and persisting for decades in others. When phantom limb pain persists for longer than 6 months, the prognosis for spontaneous improvement is poor.

### Risk factors for the development of phantom pain

Four risk factors have been identified – (i) pre-amputation pain; (ii) presence of persistent stump pain; (iii) bilateral limb amputations; and (iv) lower limb amputations. Pre-amputation pain has been a risk factor in several retrospective studies, but no association has been found in other studies. This lack of clarity may be related to the presence of recall bias associated with retrospective studies about the severity of the pre-amputation pain. Research on memory for pain would support this.

Gender, age of adults and side of amputation are not known risk factors. Phantom limb pain occurs less frequently in children and those with congenitally absent limbs.

### Phantom breast pain

Phantom pain is a well-recognized complication after limb amputation, but this phenomenon also occurs after the removal of other organs (*e.g.* breast). Phantom breast syndrome is characterized by a sensation of the persistence of the breast after its removal and has

an incidence of 25–36% after mastectomy. This syndrome encompasses a spectrum of symptoms, ranging from non-painful breast sensations to the very painful and distressing condition of phantom breast pain. The incidence of phantom breast pain ranges from 13 to 17%. Its occurrence is associated with the presence of pre-mastectomy breast pain. It is unrelated to the histological tumour type or whether the mastectomy was performed on the left or right side. The incidence of phantom breast pain is lower than after limb amputations. This may be because breasts, in contrast to limbs, do not mediate kinaesthetic sensory impulses that may be associated with the development of phantom-related phenomena, and because the somatosensory area that represents the breast is relatively small. Phantom breast pain is described as being knife-like, shooting and pricking and is initially often localized to the nipple, spreading to the entire breast during the first year after surgery. Stimuli such as emotional distress, exercise and touch often provoke this pain. Phantom breast pain often decreases in severity during the first 2 years after mastectomy.

### Pathophysiology of phantom pain

The exact mechanism for the development of phantom pain is still unknown. In general, it is believed the phenomenon is initiated by changes arising in the periphery that alter the afferent input that the brain and spinal cord receive, leading to central reorganization and changes that contribute to the development of phantom pain. Mechanisms are postulated at the peripheral, spinal and supra-spinal level.

#### Peripheral mechanisms

Alterations in the afferent nerve supply to the central nervous system arise as a result of

- ectopic discharge from afferent nerves at the amputation site and from any neuromas resulting from damaged nerves (this spontaneous discharge and firing has been linked to an upregulation of voltage-gated sodium channels in the affected nerves);
- increased sensitivity of any neuromas to mechanical and chemical stimuli;
- ectopic discharge from cells in the dorsal root ganglia, linked to the upregulation of voltage-gated sodium channels; or
- sympathetically maintained afferent input from the amputation site secondary to coupling between the sympathetic system and the sensory nervous system, similar to the mechanism occurring in complex regional pain syndrome.

#### Spinal cord mechanisms

Two main spinal cord mechanisms are proposed.

- Anatomical reorganization occurs within the spinal cord after peripheral nerve injury. The unmyelinated C-fibres involved in the conduction of pain normally synapse in lamina 1 and 2 in

the dorsal horn. Peripheral nerve injury can lead to degeneration of these unmyelinated C-fibres. The larger myelinated A $\beta$ -fibres that are normally involved in touch, pressure and proprioception sprout connections from lamina 3 and 4, where they normally synapse, into lamina 1 and 2, which were previously occupied by the C-fibres. This sprouting into the superficial lamina may contribute to the development of phantom limb pain, as previously non-painful stimuli may be experienced as painful.

- Central sensitization of dorsal horn cells occurs in response to the increased barrage of painful stimuli from the amputation site. This state of hyperexcitability leads to the development of hyperalgesia, where the patient experiences an exaggerated response to noxious stimuli. Excitatory amino acids such as glutamic acid and aspartic acid may be involved in this sensitization process, acting via *N*-methyl-D-aspartate (NMDA) receptors. Other receptor sites and neurotransmitters, such as Substance P and calcitonin gene-related peptide, may be involved.

### Supraspinal mechanisms

Cortical reorganization has been demonstrated by magnetoencephalogram studies in both humans and monkeys after limb amputation. In upper-limb amputees, the area of the somatosensory cortex corresponding to the missing limb appears to receive sensory information from other areas of the body that synapse at adjacent areas on the somatosensory cortex. The Penfield 'homunculus' (Fig. 1) shows that the face area borders the hand area. Often, upper-limb amputees, when stroked on the face, experience the simultaneous sensation of touch on the face and over the amputated digits. The speed with which these changes occur after limb amputation suggests that this reorganization is likely to be a result of unmasking of occult synapses in the somatosensory cortex, rather than direct anatomical changes. Phantom limb pain may arise from errors occurring in this cortical remapping process, leading to over-amplification of the pain experienced. There may also be errors in the sensory modalities, with touch being experienced as pain.

### Treatment of phantom pain

A range of treatments for phantom limb pain have appeared in the literature. However, there is a lack of evidence to support the efficacy of many; performing well-designed studies of sufficient power is difficult in this condition. In practice, a multidisciplinary, multimodal approach is often necessary to improve pain and quality of life in patients with phantom pain.

### Pharmacological treatment

Paracetamol, non-steroidal anti-inflammatory drugs and COX-2-specific inhibitors may be useful for treating initial postoperative pain, but they are of little use in the treatment of phantom limb pain. Opioids offer good pain relief for the immediate postoperative

period. There is evidence to support the use of opioids for the treatment of certain patients with chronic neuropathic pain. Tricyclic antidepressants (*e.g.* amitriptyline) and anticonvulsants (*e.g.* gabapentin) have been shown to be effective in the management of neuropathic pain, but most studies have not investigated phantom limb pain specifically. NMDA receptor antagonists, calcitonin and  $\beta$ -blockers have been used in the treatment of phantom limb pain. However, the evidence for their efficacy is not conclusive.

### Pre-emptive analgesia

The use of preoperative epidural anaesthesia has been investigated, and the data suggest that there is insufficient evidence of efficacy to incorporate this technique into routine practice. Two earlier trials indicated that pre-emptive epidural analgesia reduced the incidence of phantom limb pain during the first year after surgery. However, these studies had small patient numbers, no or insufficient randomization, no stratification of the severity of pre-amputation pain and a lack of blinding during assessment. Therefore, these results should be viewed with caution. A more recent well-designed study showed that pre-emptive epidural anaesthesia did not reduce the incidence of phantom limb pain.

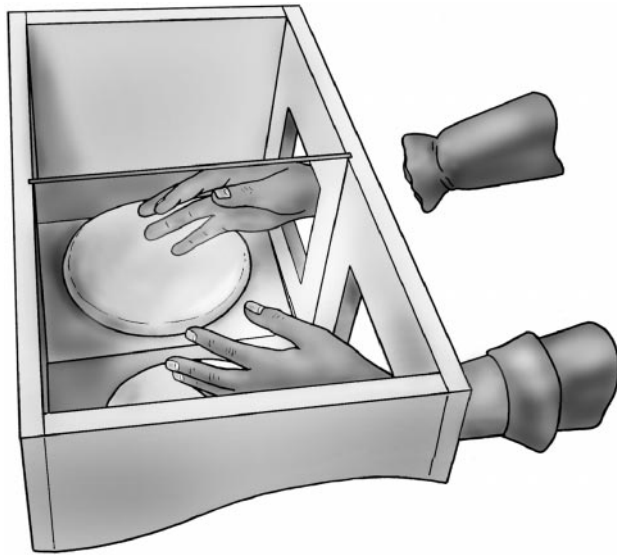
The suggested role of pre-emptive analgesia is to prevent reorganization of the nervous system occurring in response to the constant input of painful stimuli before amputation. In most cases, the amputation is often the end treatment after failed medical interventions. Patients may have had a prolonged period of pain before amputation. It may be unrealistic to expect an epidural performed 24–36 h before amputation to reverse neuronal changes that may have already taken place.

Perineural local anaesthetic blocks, although not as effective as epidural anaesthesia, can be used to provide postoperative pain relief. However, no studies have shown any reduction in the incidence of phantom limb pain with this technique.

### Physical treatments

There have been a few case reports supporting the use of acupuncture in the treatment of phantom limb pain in some patients. However, there is no strong evidence base. External heat and cold, ultrasound, transcutaneous electrical nerve stimulation, massage, adjustment of the prosthesis and manipulation of the stump have all been used with reported success.

Some patients experience involuntary movements in their phantom, such as a clenching spasm of the hand with the nails digging in to the palm. Voluntary unclenching is often effective in relieving the spasm, but patients often find this very difficult, as they have no control over the phantom. The mirror box has been used under these circumstances. It consists of a mirror placed vertically in the centre of a wooden or cardboard box, whose top and front surfaces are removed (Fig. 2). The patient places his normal hand on one side and looks into the mirror, thus creating the illusion that the amputated hand has returned and allowing the patient to visualize the unclenching of the phantom spasm.



**Fig. 2** The mirror box.

Preliminary evidence has shown this technique to be very useful in relieving these unpleasant spasms.

### Psychology

Explanation and reassurance, hypnosis, psychotherapy and cognitive behavioural therapy have all been shown to be successful in some circumstances.

### Surgery

Most surgical procedures used for phantom pain have been abandoned because of poor results. Revision of the stump is only of benefit when there is a demonstrable pathology. Stimulation of the spinal cord has been shown to decrease phantom limb pain in some cases, but there are no randomized controlled trials.

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See multiple choice questions 20–22.