Historical Considerations

• The first medical description of postamputation phenomena was reported by Ambrose Paré, a French military surgeon, in 1551. He noticed that amputees complained of severe pain in the missing limb long after amputation.

• In 1871, Civil War surgeon Silas Weir Mitchell popularized the concept of phantom limb pain and coined the term phantom limb with publication of a long-term study on the fate of Civil War amputees.
Herman Melville immortalized phantom limb pain in American literature, with graphic of Captain Ahab's phantom limb descriptions in Moby Dick.
The most commonly used terms:

- **Phantom sensation**: any sensation of the missing limb or organ except pain. *most often described in the extremities*. But can occur in any part of body: tongue, nose, breast, bladder, uterus, rectum, penis,…

- **Phantom pain**: painful sensations referred to the missing organ or limb.

- **Stump pain**: pain in the stump.

*Stump*: The part of something such as tree, tooth, arm or leg which is left after most of it has been removed (Cambridge Dictionary)

**Amputee**: a person who has had an organ cut off
Epidemiology — Phantom sensation

• Phantom limb sensation is an almost universal occurrence at some time during the first month following surgery.

• Patients generally describe the limb in terms of definite volume and length and may try to reach out with or stand on the phantom limb.

• Phantom limb sensation is strongest in amputations above the elbow and weakest in amputations below the knee.

• It is more frequent in the dominant limb of double amputees.
• The **incidence** of phantom limb **sensation** increases with the amputee's age.

• Phantom limb sensation in 85% to 98% of the amputees is seen in the first 3 weeks after amputation.

• Most phantom sensations generally resolve after 2 to 3 years without treatment, except when phantom pain develops.
Epidemiology — Phantom pain

• The incidence of phantom limb pain vary from 0% to 88%.

• In the year after amputation, 60% to 70% of amputees experience phantom limb pain, but it diminishes with time.

• The incidence of phantom limb pain increases with more proximal amputations.
• Phantom limb pain occur as early as 1 week and as late as 40 years after amputation.

• Phantom pain may diminish with time and eventually fade away. The usual course of phantom limb pain is to remain unchanged or to improve.

• Up to 56% of patients report improvement or complete resolution.
Epidemiology – stump pain

• Prevalence: up to 50% of amputees.

• Stump pain results in disuse of the limb prosthesis in approximately 50% of patients.

• The stump pain usually coincides with the development of phantom limb pain.

• Phantom limb pain is also associated with multiple pain problems in other areas of the body. (e.g. headache or pain in joints 35%, sore throat in 28%, abdominal pain in 18%, and back pain in 13% of patients)
Disability and Risk Factors

• Risk factors for phantom pain:
  phantom sensations, stump pain, pain before the amputation, cause of amputation, prosthesis use, years elapsed since the amputation.

• The most important risk factors for phantom pain is “bilateral amputation and lower limb amputation.”

• Amputees with phantom have a poorer health-related quality of life than amputees without phantom pain.
• **Sunderland**, based on the frequency and severity of pain and the degree to which pain interferes with the patient's lifestyle, proposed a classification to divide patients into four groups.
Sunderland's classification:

- **Group I** patients have mild, intermittent paresthesias that do not interfere with normal activity, work, or sleep.

- **Group II** patients have paresthesias that are uncomfortable and annoying but do not interfere with activities or sleep.

- **Group III** patients may have pain that is of sufficient intensity, frequency, or duration to be distressful; however, some patients in group III have pain that is bearable, that intermittently interferes with their lifestyle, and that may respond to conservative treatment.

- **Group IV** patients complain of nearly constant severe pain that interferes with normal activity and sleep.
Etiology

• It is believed that, throughout life, an individual's body image develops from proprioceptive, tactile, and visual inputs.

• Once a cortical representation of the body image is established, it is unchanged following limb amputation.

• The etiology and pathophysiologic mechanisms of phantom pain are not clearly defined.

• Peripheral, Central and Psychological mechanisms have been proposed.
Peripheral mechanism

• Mechanisms in the periphery, either in the stump or in the central parts of sectioned primary afferents, may play a role in the phantom limb percept.

• Peripherally, in nerve-end neuromas, *spontaneous and abnormal evoked activity* following mechanical or neurochemical stimulation is observed.

• This increased activity is assumed to be the result of a novel expression or up-regulation of *sodium channels*.
Peripheral mechanism - cont

• The increased sensitivity of neuroma to norepinephrine may, in part, explain the exacerbation of phantom pain by stress and other emotional states associated with increased catecholamine release.

• Cell bodies in the dorsal root ganglion have similar abnormal spontaneous activity and increased sensitivity to mechanical and neurochemical stimulation.

• Thus, abnormal activity from neuromas and dorsal root ganglion cell bodies may contribute to the phantom limb percept, including pain.
Mechanisms in the spinal cord

• The increased firing from **neuromas** and from **DRG cells** induce long-term changes, including:
  - spontaneous neuronal activity,
  - induction of immediate early genes,
  - increases in spinal cord metabolic activity,
  - and expansion of receptive fields.

• Spinal sensitization increased activity in NMDA receptorsystems.

• Many aspects of the central sensitization can be reduced by NMDA receptor antagonists.
Mechanisms in the spinal cord - cont

• Another event peripheral nerve transection degeneration of afferent C-fiber terminals in lamina II reducing the number of synaptic contacts in lamina II, which normally respond best to noxious stimulation.

• Consequently, central terminals of Aβ mechanoreceptive afferents, which normally terminate in deeper laminae, sprout into lamina II and may form synaptic contacts with nociceptive second-order neurons.

• As a result of this organization, generation of pain is seen with simple touch, by Aβ-fiber input.
Supraspinal or central mechanism:

- Amputation produces a cascade of events in the periphery and in the spinal cord, and these changes eventually sweep more centrally and alter neuronal activity in cortical and subcortical structures.

- Plastic changes in the thalamus are involved in the generation of chronic pain.

- A cortical reorganization have been documented after amputation.
Psychological theories

• No consistent personality disorders or clinical syndromes have shown to be increased in incidence in patients with phantom limb pain.

• However, psychological disturbances related to the loss of a limb or feelings of dependence, chronic pain and disability, may lead to many of psychological problems in these patients.

• Patients with phantom limb pain have been shown to be more rigid, compulsive, and self-reliant.
Symptoms and Signs

• Phantom sensations are painless. Patients generally describe the sensations in their phantom limb either as normal or as pleasant warmth and tingling.

• The strongest sensations come from body parts with the highest brain cortical representation, such as fingers and toes.
• “Telescoping” : patient loses sensations from the midportion of the limb, with subsequent shortening of the phantom.

• During telescoping, the last body parts to disappear are those with the highest representation in the cortex, such as the thumb, index finger, and big toe.

• **Telescoping occurs only with painless phantoms, and it is most common in the upper extremity.**

• Lengthening of the phantom may occur if pain returns.
Fig. 32.4 Illustration of telescoping of the phantom limb. The highly innervated areas (hands) remain, whereas the midportion of the phantom limb shortens in length.
• Phantom pain is primarily localized in distal parts of the missing Limb.

• Phantom pain is usually intermittent. Only a few patients are in constant pain.

• Episodes of pain occur at daily or weekly intervals, with only a few patients reporting monthly, yearly, or rare episodes.

• The duration of individual attacks may last from seconds to hours, but rarely days or longer.
The pain is usually described as **burning, aching, or cramping**. However, pain may also be described as **crushing, twisting**, **grinding**, **tingling**, **drawing**, **stabbing with needles**, **knifelike**, **sticking**, **squeezing**, **sharp**, **shocklike**, **excruciating**.

Phantom pain may mimic preamputation pain—not only in location, but also in character.

Preamputation pain may be a risk factor for phantom pain.
• Exacerbations of phantom pain may be produced by trivial, physical, or emotional stimuli.

• Anxiety, depression, urination, cough, defecation, sexual activity, cold environment, or changes in the weather may worsen phantom limb pain.

• General, spinal, or regional anesthesia in amputees may cause the appearance of phantom pain in otherwise pain-free subjects.
• In contrast to phantom pain, stump pain is often located in the stump itself and is frequently described as pressing, throbbing (لرزیدن), burning, squeezing, stabbing sensation or an electrical current.

• An additional variant of stump pain is: complaints of spontaneous movements of the stump ranging from painful, hardly visible myoclonic jerks to severe clonic contractions lasting as long as 2 days.
Physical Examination

• Physical examination is not very useful except for the trigger points in the stump to reproduce the phantom limb pain.

• Physical examination may reveal altered sensitivity in the stump.

• Neuromas are found in only 20% of patients.

• The stump may be cold, and thermography may be a useful diagnostic test if symptoms consistent with reflex sympathetic dystrophy are present.
Diagnostic Testing

• At present, no proven diagnostic test exists for evaluating phantom pain or stump pain.

• However, the patient's response to sympathetic blocks may be assessed by:
  the use of diagnostic sympathetic blocks to assist in therapeutic management.
Differential Diagnosis

• The usual course of phantom limb pain is to remain unchanged or to improve gradually.

• Up to 56% of patients report improvement or even complete resolution.

• Thus, if symptoms of phantom limb pain increase in severity or if they start after long periods of time after amputation, a differential diagnosis must be entertained.

• Some differential diagnosis:
  radicular pain, angina, postherpetic neuralgia, metastatic cancer.
• Radicular pain in the phantom limb may be associated with disk herniation.

• Increased levels of pain in the phantom limb may be triggered by new-onset herpes zoster or reactivation of herpes zoster by suppressed immunologic mechanisms.

• Angina may manifest as exacerbated phantom limb pain.

• In patients undergoing amputation secondary to malignant disease, if phantom limb pain increases significantly, metastatic disease should be evaluated.
Treatment

• Phantom limb pain often requires a multimodal approach to treatment.

• Treatment options: behavioral techniques, antidepressants, anticonvulsants, opioid and nonopioid analgesics, neural blockade, spinal cord stimulation (SCS), and motor cortex stimulation (MCS).

• No data are available to guide treatment options. (absence of evidence-based treatment guidelines)

• As a general rule, initial treatment should be low risk, low cost, and noninvasive, with more expensive and invasive treatments reserved for patients in whom conservative care fails.

• Unfortunately, treatment of phantom limb pain or stump pain is difficult and has not been very successful.
Because long-term phantom limb pain is probably the result of functional or structural changes in CNS in response to noxious somatosensory input, therapies are directed at early reduction of pain.
Prevention

• Unfortunately, initially hopeful attempts such as the use of presurgical and postsurgical epidural blockade have been questioned, and the utility of this approaches is controversial.

• Psychological preparation, drug therapy, epidural anesthesia, and regional nerve blocks, have been used to reduce the occurrence of phantom limb pain.

• At least some postamputation pain may be prevented by appropriate psychological preparation of patients.
Epidural Anesthesia

• Preoperative, intraoperative, and postoperative epidural anesthesia are associated with a significant reduction of phantom limb pain 12 months after amputation.

• However, a reduction of phantom limb pain by postoperative epidural anesthesia alone could not be confirmed on the basis of the analyzed data.

• Perioperative epidural anesthesia is effective for the prophylaxis of phantom limb pain. This technique does not completely abolish phantom limb pain, but rather increases the number of patients with a milder form of phantom pain.

• Yet, it is not known whether epidural anesthesia reduces the prevalence of phantom limb pain.
Regional Anesthesia

• With the use of perineural and intraneural blocks, either at the time of surgery or immediately postoperatively, no difference in pain is seen in the postoperative period.
Other Interventions

• Other treatments for prevention of phantom limb pain:
  - calcitonin, ketamine, intravenous lidocaine, transcutaneous electrical nerve stimulation (TENS).

• The effectiveness of all above is not clear yet.
Management of Established Phantom Pain Syndrome
Drug Therapy

• Medical therapy is the most common modality of treatment for phantom pain syndromes.

• The most frequently used classes of medications are antidepressants and anticonvulsants.
Antidepressants:
• The most effective groups are TCA and sodium channel blockers.

Anticonvulsants:
• Carbamazepine is the most commonly used.
• Carbamazepine is effective for pains that are intense, brief, lancinating type.

• Currently, Gabapentin is the most common anticonvulsant used for phantom limb pain. Other than sedation, side effects are rare, and patients become tolerant to sedation with time.

• Because gabapentin has no known long-term toxicity, monitoring of its blood levels, as with other anticonvulsants, is not necessary.
Local Anesthetics:

• Stump pain diminishes by both IV morphine and lidocaine, whereas phantom pain diminishes only by morphine.

• Mexiletine (the oral congener of lidocaine) also has been reported to be Effective.
N-Methyl-d-Aspartate Receptor Antagonists:

• Intravenous Ketamine can reduce pain, hyperalgesia, and “wind-up”–like pain in stump and phantom pain.

• But Memantine (another NMDA receptor antagonist used for Alzheimer’s disease) fails to reduce pain in phantom limb pain.

• Oral Dextromethorphan can effectively reduces phantom limb pain.

• Capsaicin may be used as a treatment for phantom limb pain.
Beta-Adrenergic Blockers and Benzodiazepines:

• Use of them are still unknown and controversial.
**Opioids:**

- In phantom pain, **opioids can be used safely with efficacy for years with a limited risk of drug dependence.**

- They may also potentially influence cortical reorganization.

- Further, **patients undergoing amputation related to systemic medical diseases have only a 42% 5-year survival rate; thus, the risk of opioid addiction may be weighed against quality-of-life issues.**

- **Tramadol** provides excellent and stable phantom limb and residual limb pain control, with no major adverse events.

- **Morphine sulfate** can significantly reduce pain in phantom limb pain.
**Neural Blockade:**

- Although physicians performing these blocks in the treatment of phantom limb pain report a high success rate, it has not been substantiated.

- These blocks include:
  - trigger point injections, neurolytic sympathetic blocks, stump injections, sympathetic blocks, peripheral nerve blocks, epidural or subarachnoid blocks.

- Only 14% of patients with phantom limb pain report a significant temporary change.
- Less than 5% report a large permanent change or cure.

- The use of neural blockade in the treatment of phantom limb pain is largely based on anecdotal reports in the literature.
• **Lesions of the dorsal root entry zone** provide long-term pain relief in patients with phantom limb.

• **Botulinum toxin A injections**
  
  • Muscle tension, resulting from cortical reorganization, may contribute to phantom pain.
  
  • Botulinum toxin A - by muscle relaxation in the stump or through inhibition of the release of various neurotransmitters - may lead to analgesia.
Other treatment modalities:

• **Neuromodulation:** TENS, SCS, DBS

• **Neurosurgical Techniques:** intrathecal implantable devices, stereotactic thermocoagulation lesions, cordotomy

• **Stump Revision:** Patients with phantom limb issues related to the stump (vascular insufficiency, infection, extensive neuromas) may undergo stump revision. (benefit in 50% of patients)

• **Physical Therapy:** useful, especially the educational aspect with attention to stump and preparation for prosthesis.

The reason is that phantom limb pain is most commonly seen in patients who are unable to use a prosthesis within the first 6 months following amputation.
Other treatment modalities- cont

• **Acupuncture**: provide Short-term (but no long term relief) from phantom limb pain.

• **Electroconvulsive Therapy (ECT)**: (?)

• **Psychological Therapies**: Relaxation training with or without biofeedback or hypnosis can decrease anxiety levels, increase pain relief but **relapses occur soon after the discontinuation of the treatment**.
What is in 2021 articles?
Clinical updates on phantom limb pain

Joachim Erlenwein, Martin Diers, Jennifer Ernst, Friederike Schulz and Frank Petzke

Abstract

Introduction:

Most patients with amputation (up to 80%) suffer from phantom limb pain postsurgery. These are often multimorbid patients who also have multiple risk factors for the development of chronic pain from a pain medicine perspective. Surgical removal of the body part and sectioning of peripheral nerves result in a lack of afferent feedback, followed by neuroplastic changes in the sensorimotor cortex. The experience of severe pain, peripheral, spinal, and cortical sensitization mechanisms, and changes in the body scheme contribute to chronic phantom limb pain. Psychosocial factors may also affect the course and the severity of the pain.
• The scientific evidence for best practice is weak.
• Various clinical reports describing the polypragmatic use of drugs and interventional techniques.

• Approaches to restore the body scheme and integration of sensorimotor input are of importance.

• Modern techniques, including virtual reality, offer an exciting supplement to already established approaches.

• Targeted prosthesis care helps to obtain or restore limb function and at the same time plays an important role reshaping the body scheme.
Gabapentin for phantom limb pain after amputation in pediatric oncology: a systematic review protocol

Shuang Jiang, Meng-meng Zhou, Rong Xia, Jing-hui Bai & Li-hui Yan

Systematic Reviews 10, Article number: 26 (2021) | Cite this article

Abstract

Background

Phantom limb pain (PLP) is a prevalent problem for children after amputation because of the chemotherapy treatment. Gabapentin is a potential option to manage PLP after amputation in pediatric oncology. However, no systematic review specifically investigated this topic. Thus, this study aims to appraise the efficacy and safety of gabapentin for post-amputation
This study represents the first systematic review to examine the efficacy and safety of gabapentin for PLP after amputation in children with oncology. We expect our results that should allow us to draw beneficial conclusions about the efficacy and safety of gabapentin for PLP after amputation in pediatric oncology, which may benefit both clinicians and future studies.
Prevalence and incidence of phantom limb pain, phantom limb sensations and telescoping in amputees: A systematic rapid review

Anna Stankevicius, Sarah B. Wallwork, Simon J. Summers, Brenton Hordacre, Tasha R. Stanton

First published: 03 September 2020 | https://doi.org/10.1002/ejp.1657 | Citations: 1

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Read the full text ➤
• Lifetime prevalence of phantom pain was the highest, with most individuals experiencing some type of phantom phenomena at some point post-amputation.

• Most amputees will experience phantom limb pain (PLP) and phantom limb sensations (PLS):
  ✓ high PLP incidence 1-year post-amputation (82%);
  ✓ high lifetime prevalence for PLP (76%–87%) and PLS (87%).
  ✓ Approximately 25% of amputees will experience telescoping.
Thx for your attention

Dr AmirAziz Saif
فروردین ماه 1400