Phantom Limb Pain

Paul S. Tumber, MD FRCPC
Assistant Professor of Anesthesiology
Toronto Western Hospital
Pain Consultant, UHN and
Wasser Pain Clinic, Mt. Sinai Hospital
paul.tumber@uhn.ca

Disclosure

• Nothing to disclose in terms of influence on this presentation
• Have recently given a lecture on Trigger Points for Wasser Pain Centre and given an unrestricted educational honorarium by Purdue

Objectives

• Develop an understanding about how phantom limb pain presents
• Review the different strategies used to treat phantom limb pain

Phantom Limb Pain (PLP)

Incidence: 50-85%
• Most studies report association with pain levels prior to amputation; with trauma the association may be with the amount of postoperative pain.
• Half of patients start to experience pain in the first 24h, and another 25% experience pain in the first week. Uncommon for it to start years after amputation.
• Frequency and severity of episodic pain tends to decrease over time: 5-10% with severe persistent pain
• Stump pain: persists in 5-10%. If present, then more likely to have PLP
• Also uncommon to have PLP but no phantom sensation
• All patients should have good perioperative analgesia but it is not conclusive that this will prevent PLP

Phantom Sensations

1. Kinetic
   – Spontaneous or willed sensation of movement
2. Kinesthetic
   – Size, shape and position of the missing part
3. Exteroceptive
   – Touch, temperature, pressure, itch, vibration
   – Some would include phantom pain in this category

History

Ambrose Paré (1551)
– French military surgeon
– Technique of amputation
– First description of post-amputation pain

Silas Weir Mitchell (1871)
– Neurologist
– Observed Civil war veterans
– "phantom limbs"

Weeks et al. The Neurologist 16(5); 2010
Characteristics

- Description: burns, cramps, tingles or pins and needles, electric shocks, itches, stabs
- May have uncomfortable feeling of pre-amputation state of distal limb (e.g. clutching or cramping or compression)
- Timing: Can be present for few seconds to 1-2h but NOT usually constant
- Worse with stress, attention, peripheral stimulation of neuroma, etc.

Etiology: Theories

- Peripheral: Neuroma, sensitization, DRG
- Spinal Cord: neuroplasticity, sympathetic nervous system and wind-up phenomenon
- Brain:
  - Cortical remapping and neuroplasticity
  - 'Learned paralysis' of phantom
  - Neuromatric theory
  - Sensory, affective and cognitive aspects
  - Proprioreceptive memory
    - e.g., Limb position under regional anesthesia

The Dark Side of Chronic Pain:

- Psychological: somatically focused, depressed, anxious, irritable, sleep-deprived + grief, self-pity, PTSD, catastrophizing
- Dysfunction: personal, job, social, spouse
- Myofascial pain +
- Deactivation, deconditioned, weight gain
- Secondary gain issues: WSIB, family
- Frustration with the medical system
- Enigma and Stigma

http://www.gb42.com/ynot_The_Pain_Exhibit.html
### PATIENT ASSESSMENT

- Psychologic Factors?
- Prosthesis Limb Pain?
- Prosthesis fit and function
- Infection
- Edema
- Skin abrasions
- Neuroma
- Musculoskeletal issues (bursa, ligament, bone spur)
- Other: radiculopathy, vascular, CRPS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical</strong></td>
<td>Mainstay</td>
</tr>
<tr>
<td>Psychological</td>
<td>Education, support</td>
</tr>
<tr>
<td>Pharmacologic</td>
<td>Multimodal</td>
</tr>
<tr>
<td>Interventional/Surgical</td>
<td>Limited role</td>
</tr>
</tbody>
</table>

- NO easy, single answer as to best treatment
- Limited and sometimes conflicting evidence for all of the possible modalities
- Pharmacotherapy is not effective in many cases

### Treatment Comments

<table>
<thead>
<tr>
<th>Physical</th>
<th>Mainstay of persistent pain management.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Encourage active physical therapy</td>
</tr>
<tr>
<td></td>
<td>Use of new prosthesis</td>
</tr>
<tr>
<td></td>
<td>Mirror therapy</td>
</tr>
<tr>
<td></td>
<td>Desensitization (if allodynia)</td>
</tr>
<tr>
<td></td>
<td>Massage (lacr., soft tissue)</td>
</tr>
<tr>
<td></td>
<td>TENS Unit</td>
</tr>
<tr>
<td></td>
<td>Hot/cold</td>
</tr>
</tbody>
</table>

Psychological

- Education, Reassurance, Support.

Pharmacologic

- Multimodal

Interventional/Surgical

- Limited role

### Drugs to treat phantom limb pain in those with amputations

Various medications have been tried in phantom limb pain but good treatment courses to be anachronistic. Whether opioids, N-methyl-D-aspartate (NMDA) receptor antagonists (e.g. ketamine, remifentanil, dextromethorphan), anticonvulsants, antidepressants, calcitonin and anesthetics are effective in improving outcomes that include pain, sleep, mood, daily activities, quality of life, satisfaction and safety is not clear and long-term, certain outcomes. A meta-analysis of 15 studies concluded that the effectiveness of anticonvulsants is not superior to placebo. However, there are no randomized controlled trials to support the use of these drugs. There is limited evidence for the use of other agents such as ketamine and dextromethorphan. These studies usually included small numbers of study participants and lacked long-term efficacy and safety data. Large, high-quality, randomized controlled trials that are important to patients are needed to make firm recommendations on the best pain relief for this patient population.

Multimodal Pharmacotherapy

Acetaminophen
NSAIDs
Opioids
Anticonvulsants
Antidepressants
Cannabinoids
Topical Agents

Neuropathic pain: CANADA

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIRST LINE</td>
<td>Tricyclic Antidepressants Nortriptyline, Desipramine</td>
</tr>
<tr>
<td></td>
<td>Anticonvulsants Gabapentin, pregabalin (carbamazepine: tic douloreux)</td>
</tr>
<tr>
<td>SECOND LINE</td>
<td>SNRI Duloxetine, venlafaxine</td>
</tr>
<tr>
<td>THIRD LINE</td>
<td>Tramadol Opoids</td>
</tr>
<tr>
<td>FOURTH LINE</td>
<td>Cannabinoids Sativex buccal spray, dronabinol</td>
</tr>
<tr>
<td></td>
<td>Topical lidocaine</td>
</tr>
<tr>
<td></td>
<td>Methadone</td>
</tr>
<tr>
<td></td>
<td>Other anticonvulsants Lamotrigine, topiramate, valproic acid</td>
</tr>
</tbody>
</table>


Neuropathic pain: IASP

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIRST LINE</td>
<td>Tricyclic Antidepressants Nortriptyline, Desipramine</td>
</tr>
<tr>
<td></td>
<td>Anticonvulsants Gabapentin, pregabalin</td>
</tr>
<tr>
<td></td>
<td>SNRI Duloxetine, venlafaxine</td>
</tr>
<tr>
<td>SECOND LINE</td>
<td>Tramadol Topical Lidocaine/ Capsaicin 8%</td>
</tr>
<tr>
<td>THIRD LINE</td>
<td>Opioids Botulinum Toxin</td>
</tr>
<tr>
<td></td>
<td>Caution with use Preliminary evidence</td>
</tr>
</tbody>
</table>


Gabapentinoids

<table>
<thead>
<tr>
<th>Trade name</th>
<th>Initial Dose</th>
<th>Max dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin</td>
<td>Neurontin</td>
<td>Start low dose (100-300mg tid), increase by 300mg every three days.</td>
<td>3600mg/day</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Lyrica</td>
<td>Start 25 – 50 mg tid, increase by 75mg every 7 days</td>
<td>600mg/day</td>
</tr>
</tbody>
</table>

NOTES
- If the patient wishes to stop the medication then taper over one week to avoid withdrawal phenomena
- Warn patients of sedation and driving/operating machinery
- Elderly can become confused
- May also improve sleep, reduce concurrent anxiety and is used in certain perioperative pain management regimens
- Pregabalin is indicated in Canada for neuropathic pain from diabetic neuropathy, post-herpetic neuralgia, spinal cord injury as well as for fibromyalgia

Other anticonvulsants:

- Carbamazepine
  - Remains drug of choice for trigeminal neuralgia
  - Can be toxic to liver/hematologic system, beware drug interactions, monitor bloodwork regularly
  - Oxcarbazepine (Trileptal), a ketoanalogue of carbamazepine with less adverse effects
- Lamotrigine
  - Can cause serious rash (Stevens-Johnson syndrome)
  - Need to start low and escalate slowly to reduce risk
- Topiramate
  - Used in neuropathic pain, migraine prophylaxis
  - Side effects include weight loss, cognitive difficulties, possible renal stones (need to monitor serum bicarbonate)
  - Few drug interactions
- Valproic acid
  - Not commonly used. Need to monitor bloodwork (liver, amylase, hematologic)

Antidepressants

- Serotonin Noradrenaline Reuptake Inhibitors
  - Duloxetine is FDA-approved in diabetic neuropathy and fibromyalgia.
  - SSRIs are not as useful in neuropathic pain.

<table>
<thead>
<tr>
<th>Trade name</th>
<th>Initial Dose</th>
<th>Max dose</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlaxafine</td>
<td>Effexor</td>
<td>37.5mg/d</td>
<td>225mg/d</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Cymbalta</td>
<td>60mg/day</td>
<td>120mg/d</td>
</tr>
</tbody>
</table>
  - Incr bleeding risk
  - Hyponatremia |
Opioids: Concerns

- Sleep apnea
- Tolerance vs. pseudo tolerance
- Opioid induced hyperalgesia
- Addiction vs. pseudo addiction / dependence
- Sedation (incl. risk of falls in elderly)
- GI side effects (esp. constipation)

OPIOIDS: Stepped approach

- Mild to Moderate Pain
  - First line: Codeine or tramadol
  - Second line: morphine, oxycodone, hydromorphone

- Moderate to Severe Pain
  - First line: morphine, oxycodone, hydromorphone
  - Second line: fentanyl transdermal patch
  - Third line: methadone

Adverse Effects of Opioids

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>Tends to reduce with time. Start opioids at low dose. Consider antiemetics, opioid rotation.</td>
</tr>
<tr>
<td>Constipation</td>
<td>Does not resolve with time. All patients need to be warned and started on stool softener, bowel stimulant etc.</td>
</tr>
<tr>
<td>Somnolence</td>
<td>If sedated, patients should not drive/operate machinery when starting or increasing doses. Beware of this in elderly especially. Beware coadministration of opioids with other sedatives (synergistic effect)</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Rare esp. if opioids are titrated. Beware patients with sleep apnea, benzodiazepines. Need intravenous naloxone for rapid reversal.</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>Hypogonadism, amenorrhea</td>
</tr>
<tr>
<td>Opioid induced hyperalgesia</td>
<td>Paradoxical hyperalgesia. May be seen with chronic administration of high dose opioids.</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Most often a central nervous system effect rather than allergy or histamine release.</td>
</tr>
</tbody>
</table>

Summary

Consider the outcome of your pain management:

1. Reduction in pain score
2. Reduction in side effects
3. Improved function (work, leisure, social, etc)
4. Improved quality of life/ wellbeing/ satisfaction
5. Reduced health care utilization / cost
Selected References:
