Neuropathic Pain
Where Guidelines Fail

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Neuropathic pain; definition

“pain due to an abnormal function of a neuron in the peripheral or central nervous system in the absence of a noxious stimulus”
What is neuropathic pain?

- Pain initiated or caused by a primary lesion or dysfunction in the peripheral or central nervous system\(^1\)

- The painful region may not necessarily be the same as the site of injury – pain occurs in the neurological territory of the affected structure (nerve, root, spinal cord, brain)

- Almost always a chronic condition (e.g. postherpetic neuralgia [PHN], central post stroke pain [CPSP])\(^2\)

- Responds poorly to conventional analgesics\(^3\)

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Problems in the treatment of neuropathic pain

- Failure to diagnose neuropathic pain
  - Undertreatment
- Efficacy
- Pain associated symptoms
  - Sleep, mood, social aspects
- Side effects
- Reliance on ineffective drugs
- Reliance on monotherapy
- Expense of non-pharmacological treatment
Diagnosis

- Underdiagnosis
- Undertreatment
Prevalence of chronic pain across Europe

1. Pain In Europe – A Report – Janet Fricker in association with Mundipharma International Ltd.

Prevalence (n=46,394)

- Norway: 30%
- Poland: 27%
- Italy: 26%
- Belgium: 23%
- Austria: 21%
- Finland: 19%
- Sweden: 18%
- Netherlands: 18%
- Germany: 17%
- Israel: 16%
- Denmark: 16%
- Switzerland: 15%
- France: 13%
- Ireland: 13%
- UK: 11%
- Spain: 11%
UK survey of pain of predominantly neuropathic origin

- 6000 questionnaires were mailed
  - 3002 questionnaires were completed (52.4%)
  - 2957 questionnaires could be assessed for presence or absence of chronic pain
- 241 had a positive S-LANSS score (8.2%; 95% CI: 7.2–9.2)

Diagnosis of neuropathic pain

- **History**
  - Burning lancinating dysaesthetic pain
  - Paraesthesia, hyperaesthesia, anaesthesia

- **Examination**
  - Hyperalgesia, allodynia
  - Anaesthesia, hypoaesthesia

- **Validated scoring systems**
  - LANSS
  - Paindetect
PAIN QUESTIONNAIRE

Date: [ ]
Patient: [ ]
Last name: [ ]
First name: [ ]

How would you assess your pain now, at this moment?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the strongest pain during the past 4 weeks?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the pain during the past 4 weeks on average?

0 1 2 3 4 5 6 7 8 9 10

none max.

Mark the picture that best describes the course of your pain:

- Persistent pain with slight fluctuations
- Persistent pain with pain attacks
- Pain attacks without pain between them
- Pain attacks with pain between them

Does your pain radiate to other regions of your body? Yes [ ] No [ ]

If yes, please draw the direction in which the pain radiates.

Please transfer the total score from the pain questionnaire:

Total score [ ]

Please add up the following numbers, depending on the marked pain behavior pattern and the pain diathesis. Then total up the final score:

- Persistent pain with slight fluctuations
  -0 if marked, or
- Persistent pain with pain attacks
  -1 if marked, or
- Pain attacks without pain between them
  +1 if marked
- Pain attacks with pain between them
  +1 if marked

Radiating pains?

+2 if yes

Final score [ ]

Screening Result

Final score [ ]

nociceptive unclear neuropathic

A neuropathic pain component is unlikely (< 15%)
Result is ambiguous, however a neuropathic pain component can be present
A neuropathic pain component is likely (> 90%)

This sheet does not replace medical diagnostics. It is used for screening the presence of a neuropathic pain component.


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Neuropathic pain: Clinical assessment

- **THE S-LANSS PAIN SCORE** (Leeds Assessment of Neuropathic Symptoms and Signs)

- **Five symptom items and two examination items.**
  - 1. In the area where you have pain, do you also have 'pins and needles', tingling or prickling sensations?
  - 2. Does the painful area change colour
  - 3. Does your pain make the affected skin abnormally sensitive to touch?
4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still?

5. In the area where you have pain, does your skin feel unusually hot like a burning pain?

6. Gently rub the painful area with your index finger. How does this rubbing feel in the painful area?

7. Gently press on the painful area with your finger tip. How does this feel in the painful area?
Whatever the definition it’s difficult to treat

*however*

Pharmacotherapy for neuropathic pain is highly evidence based
Conventional drugs

- Tricyclic antidepressants
  - Amitriptyline
  - Nortryptiline
  - Dosulepin

- Antiepileptic drugs
  - Carbemazepine
  - Oxcarbazepine
  - Na Valproate
Gabapentin and Pregabalin

- Bind to $\alpha_2$ subunit of Ca$^{++}$ channel
- Reduce pain, allodynia, hyperalgesia

Pregabalin: 11 RCTs n=2887 NNT 4
Topical Agents

- Lidocaine 5% patch
- Capsaicin 0.075% cream
- (Capsaicin 8% “Qutenza” Astellas)
Efficacy: Lack of efficacy?
Reduction in pain scores; is it enough?

Change in mean pain score from baseline

Baseline pain score = 6.7

Inneffective Drugs: Opioids?
Opioids in neuropathic pain

- Poor evidence for codeine, fentanyl, methadone, buprenorphine
- Better evidence for morphine, oxycodone, tramadol
- Problems with side-effects
- Need for protocols to avoid misuse
Tramadol

- Noradrenaline and Serotonin reuptake inhibitor
- Weak $\mu$-receptor agonist
- 5 studies show efficacy in NP
Monotherapy vs combination therapy
Drugs in combination

- Morphine plus Gabapentin (vs active placebo or either alone)
  - improved analgesia
  - lower doses
  - less side effects

NEJM. 2005 Mar 31;352(13):1324-34.
New drugs
Antidepressants: Duloxetine

- Mixed serotonin and NA uptake inhibition (SNRI)
- Large study of duloxetine in diabetic neuropathic pain: NNT 4
- Less sedation than tricyclic antidepressants

Goldstein, Pain, 2005, Volume 116, Issue 1, Pages 109-118
Qutenza: 8% topical capsaicin (Astellas)

- Prolonged efficacy (>16 weeks) in
  - PHN
  - HIV associated NP
- TRPV1 receptor agonist
- Reduction in sub-epithelial nociceptive nerve endings
- Application is hospital based
- ? Cost

M. Backonja *The Lancet Neurology*, 2008;7 12: 1106-1112

D. M. Simpson *Neurology* 2008;70: 2305-2313
Pain related effects

- Sleep
- Mood
- Relationships
- Activity
- Work
The 3 R’s in the treatment of chronic pain

- Reassurance (psychotherapy)
- Relief (pharmacotherapy)
- Rehabilitation (physiotherapy)

Adapted from: Raja SN, Grabow TS. Anesthesiology 2002; 96(5): 1254–1260
Treatment should involve a three-pronged approach

- The ultimate treatment goal is pain relief and restoration of function and health
- No single therapeutic modality achieves this goal in all patients
- Physiotherapy, pharmacotherapy and psychotherapy all play a role

Adapted from: Raja SN, Grabow TS. Anesthesiology 2002; 96(5): 1254–1260
Evidence based guidelines

- Finnerup et al 2005
- European Federation of Neurological Societies (EFNS) 2006 & 2009
- National Institute of Clinical Excellence (NICE) UK 2010
Perpheral Neuropathic pain

Postherpetic neuralgia/ focal Neuropathy

yes

Lidocaine patch

no

TCA contraindicated

yes

Gabapentin/Pregabalin

no

TCA

Gabapentin/Pregabalin

Tramadol/Oxycodone

After Finnerup NB et al 2005 Pain 118
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2006 EFNS European Journal of Neurology 13, 1153–1169
Painful Diabetic Neuropathy

First Line
• Duloxetine or Amitriptyline

Second Line
• Change or combine drugs
• Consider Pregabalin

Other Neuropathic Pain Conditions

First Line
• Amitriptyline or Pregabalin
• Consider Nortript/Imipr

Second Line
• Change or combine drugs

Early review for titration or change

Consider referral to Pain Clinic

If long term opioid considered referral to Pain Clinic
Problems

- Failure to diagnose neuropathic pain
  - Undertreatment
- Efficacy
- Pain associated symptoms
  - Sleep, mood, reduced exercise, social aspects
- Side effects
- Reliance on ineffective drugs
- Reliance on monotherapy
- Expense of non-pharmacological treatment
Solutions

- Better and earlier diagnosis
- Primary care diagnosis and treatment
- Early referral to pain clinic where ineffective
- Early dose titration and review of treatment
- Change drugs where ineffective
- Combine drugs where ineffective
- Multidisciplinary care
- New treatments