Neuropathic pain

Possible neuropathic pain - clinical presentation

History and examination

Red flag and 4D risk assessment

If criteria are met, refer urgently to specialist

Explain condition and provide information and self-help options

Develop and agree a management plan with the patient including ongoing assessment

Complex regional pain syndrome (CRPS)

Go to complex regional pain syndrome

First-line treatment

Topical treatment for focal neuropathies

Second-line treatment

Add in tramadol as third line treatment

Review if not improved, and consider referral for further specialised diagnostic testing

Refer for specialised diagnostic testing

Confirm diagnosis and consider multidisciplinary team (MDT) referral

Develop and agree a management plan with patient including ongoing assessment

Consider interventional pain therapies and medications that require specialised supervision

Provide a multidisciplinary review to consider treatment options

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Neuropathic pain

1 Care map information

Quick info:
Scope:
- initial assessment and management of pain in adults with neuropathic pain across non-specialist and specialist care, including:
  - early assessment
  - evidence-based intervention of appropriate management based on diagnosis and assessment
  - self-management
Out of scope:
- tertiary care management
- initial assessment and management of pain in adolescents and children
Definition:
- pain caused by a lesion or disease affecting the somatosensory nervous system [15]
Prevalence:
- pain with neuropathic characteristics or of predominantly neuropathic origin has been found to range from 3.3% to 8.2% [16]
General principles of pain management:
- improved recognition and holistic management of pain to avoid inappropriate treatment with high doses of analgesics
- the majority of treatment can be delivered in non-specialist care but early recognition of the need for multidisciplinary and or specialist pain services input is required to reduce delays in treatment and therefore improve outcomes
- psychological and social issues need to be identified and addressed in parallel with appropriate pharmacotherapy and any physiotherapy to ensure effective care

References:
Please see the care map's provenance.

2 Information resources for patients and carers

Quick info:
Recommended resources for patients and carers produced by organisations certified by The Information Standard:
- Arthritis Care (URL) at http://www.arthritiscare.org.uk
- 'Chronic pain – a self-help guide' (URL) from Patient UK at http://www.patient.co.uk
- 'Drug treatments for neuropathic pain' (PDF) from the National Institute for Health and Clinical Excellence (NICE) at http://www.nice.org.uk
- 'Neuropathic pain' (URL) from the Brain and Spine Foundation at http://www.brainandspine.org.uk
- 'Neuropathic pain' (PDF) from Patient UK at http://www.patient.co.uk

For details on how these resources are identified, please see Map of Medicine’s document on Information Resources for Patients and Carers (URL).

The following resources are recommended by the British Pain Society [1]:
- telephone advice through NHS Direct
- written information from a variety of charities or locally from the pain service
- information on Expert Patients Programme (EPP) – this should be given to everyone who has a chronic condition as the EPP website includes details of all programmes that are running each month
- Welsh Backs
- Sheffield Backs
- Pain Concern
- Action on Pain
- National Exercise Referral Scheme (NERS)
- Health at Work advice line – this is for small and medium-sized businesses with easy access to professional occupational health telephone advice
- Understanding and Managing Pain: information for patients (URL) from the British Pain Society
- 'Airing Pain' (URL) – Radio Programme from Pain Concern covering all aspects of pain:
  - all programmes can be accessed via the website
  - access to leaflets on chronic pain and drug treatments
  - a helpline
  - forums
- Backcare (URL) – provides information sheets and booklets on a whole range of back care related issues:
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- helpline
- forums
- local groups
- information on local and regional resources

* The Expert Patients Programme (URL) – provides self-management courses for long-term conditions
* The pain toolkit (URL) – self management tool for people in chronic pain
* National Osteoporosis Society (URL) – provides:
  - information
  - support groups
  - a helpline
* Action on Pain (URL) – provides:
  - information
  - a helpline
* Arthritis Research UK (URL) – provides:
  - patient information
  - research information
  - advice on medication may also be sought from local community pharmacists

3 Updates to this care map

Quick info:
Date of publication: 31-Oct-2013
Pharmacological information regarding starting pregabalin has been updated following feedback from British Pain Society.
Please see the care map's Provenance for additional information on references, accreditations from national clinical bodies, contributors, and the editorial methodology.

Date of publication: 19-Nov-2012
This care map has been drafted using the Map of Medicine editorial methodology (URL) and represents best clinical practice according to the highest quality evidence available, including the following guidelines:


Further information was provided by the following references, including practice-based knowledge: [1,2-11,14,15,18-20,22-31,34]
Please see the care map's Provenance for additional information on references, accreditations from national clinical bodies, contributors, and the editorial methodology.

4 Pharmacological information

Quick info:
Principles of initial pharmacological management for patients [1]:

- pharmacology is one method of analgesia – other non-pharmacological methods (eg self-management strategies and physiotherapy) should also be explored with patients, as an over-reliance upon medication can be misplaced and send the wrong message to patients
- identify and treat, where possible, specific sources of pain and base the initial choice of medication on the severity and type of pain [2-11]
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• agree goals of therapy before prescribing and adjust choice of medications to meet the needs of the individual [12]
• discuss risks and benefits of potential medications, particularly discuss potential side effects
• give medication an adequate therapeutic trial and agree this period with the patient before initiating further treatment – some medications may require dose titration and optimisation over several weeks before reaching maximum therapeutic effect
• consider rational polypharmacy – appropriate use of analgesic combinations may produce improved efficacy and fewer adverse effects, as lower doses of individual medication may be required
• provide specific guidance on opioid analgesia – see British Pain Society guidelines [13,14]
• tricyclic antidepressant (TCA) may be useful where sleep is a problem even if the pain is not neuropathic in origin:
  • NB: this use of tricyclic antidepressants (TCAs) is outside of its product licence in the UK
Principles of managing ongoing analgesic therapy include the 4 'A's [1]:
• Analgesia – is the medication still providing useful pain relief?
• Adverse effects – what side effects is the patient experiencing and can these be managed more effectively?
• Activity – does the patient maintain suitable physical and psychosocial functioning?
• Adherence – is the patient taking medication as agreed in the management plan?

Useful websites recommended by the British Pain Society include:
• UK Medicines Information
• Royal Pharmaceutical Society of Great Britain
• UK Clinical Pharmacy Association
• Primary Care Pharmacists Association
• PRODIGY
• British Pain Society
• Pain Community Centre

References:
Please see the care map's provenance.

5 Possible neuropathic pain - clinical presentation

Quick info:
If pain distribution is neuroanatomically plausible and history suggests relevant lesion or disease, neuropathic pain is possible [16].
Neuropathic pain develops as a result of damage to, or dysfunction of, the system that normally signals pain [17]:

• common causes include:
  • painful diabetic neuropathy [17]
  • post-herpetic neuralgia [17]
  • trigeminal neuralgia [17]
  • radicular pain [17]
  • pain after surgery [17]
  • neuropathic cancer pain, ie chemotherapy-induced neuropathy and neuropathy secondary to tumour infiltration [17]
  • HIV neuropathy [18]
• patient may experience [17]:
  • altered pain sensation
  • areas of numbness or burning
  • continuous or intermittent evoked or spontaneous pain

References:
Please see the care map's Provenance.

6 History and examination

Quick info:
Clinical examination is a crucial part of the diagnostic process of neuropathic pain, aiming at finding possible abnormalities relating to a lesion of the somatosensory system [16]:
• sensory testing is the most important part of this examination and includes testing of touch, vibration, pinprick, cold and warmth
• no 'gold standard' is available to label a specific pain within an area of sensory abnormalities as neuropathic pain – use clinical judgement based on the outcome of a comprehensive clinical approach
• negative or positive sensory signs, confined to innervation territory of the lesioned nervous structure, are suggestive of neuropathic pain

Consider potential value of self-completion neuropathic pain questionnaires [18]:
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- eg LANSS, painDETECT, DN4, ID Pain
- quick, simple, and can assist in supporting or refuting the likelihood of neuropathic pain, but are not in themselves definitive
- can be used in specialist or non-specialist care settings
- may also identify some symptoms that may not easily be volunteered or asked about (eg itch, crawling sensation, running water sensation)

See ‘Pain – initial assessment and early management’ care map for more information.

References:
Please see the care map's Provenance.

7 Red flag and 4D risk assessment

Quick info:
4D risk assessment [1]:
- Disability
- Distress
- Diagnostic difficulties
- Drug problems
Refer to specialist urgently if any of the following criteria are met [17]:
- there is diagnostic uncertainty
- patient has severe pain
- pain significantly limits daily activities
- the underlying health condition has deteriorated
Continue to work through neuropathic flow chart whilst waiting [1].

NB: Patients who are referred with red flags to secondary care, but do not go on to have surgical intervention (eg due to symptoms settling or changing) are referred back into the primary care pathway and may still need access to MDT referral. See 'Confirm diagnosis and consider multidisciplinary team referral' care point [18].

This information was drawn from the following references:

References:
Please see the care map's Provenance.

8 Explain condition and provide information and self-help options

Quick info:
Explain condition [1]:
- patient information is known to improve patient experience and involvement with their care [19]
- address people's concerns about understanding their pain with the aim of reducing their fears about pain [1]
- use patient information leaflets and self guided websites, eg [1]:
  - British Pain Society (URL)
  - Neil Berry's online audio descriptions of pain (http://www.paincd.org.uk)
  - Pain Concern (URL) is a charity run by pain sufferers providing support for people living with pain and those that care about them
  - the Neuropathy Trust (URL) is a charitable organisation with a website dedicated to helping people with neuropathic pain
Patient education should commence early in the process and certainly at the first assessment [1]:
- it should not just be considered as giving patients information in the form of leaflets, but the health professional needs to ask the patient how they best learn in order to improve their experience and involvement in care
- self-care and management underpins all activities within this pathway and should be considered alongside each care point
- commissioners should commission structured education and appropriate resources and all healthcare professionals (HCPs) should be able to refer patients to the peer support offered by Third Sector Organisations
- self-management information should be available even before the patient has accessed the service and can then be used as an adjunct to treatment after initial assessment – this is especially important for patients waiting to see specialist health professionals

References:
Please see the care map's Provenance.

9 Complex regional pain syndrome (CRPS)
Neuropathic pain

Quick info:
Complex regional pain syndrome (CRPS) is:
• defined as continuing regional pain out of proportion to the severity of the inciting event and beyond the normal time frame expected following the event [20]
• thought to be caused by abnormal healing following a nerve or soft tissue injury [35]
• a diagnosis of exclusion [21]

Rapid therapy for CRPS is likely to reduce long term disability [1]:
• refer for urgent specialist assessment for intensive physiotherapy and management [1]
• also consider access to psychological pain management to support improved condition management [18]
• actively manage with drugs from neuropathic pain pathway [1]
• a definition of recovery from CRPS has not yet been agreed [21]:
  • limb signs such as swelling, sweating, and colour changes usually reduce with time, even where pain persists
  • such reduction of limb signs is in itself not 'recovery'
  • where pain persists, the condition is best considered to be active

References:
Please see the care map's Provenance.

11 Develop and agree a management plan with the patient including ongoing assessment

Quick info:
Describe the options for treatment available to allow for patient choice [1]:
• self-help
• medication
• cognitive behavioral multidisciplinary pain management

There are considerable numbers of studies supporting cognitive behavioural therapy (CBT) in chronic pain but very few looking at the subset with neuropathic pain [22].
Consider managing patient on other pathways as clinically indicated, eg for radicular pain see 'Spinal pain' care map [1].

References:
Please see the care map's Provenance.

12 First-line treatment

Quick info:
First-line treatment:
• National Institute for Health and Clinical Excellence (NICE) guidelines were produced for non-specialist pharmacological management [17]
• these have been supplemented by more recent systematic reviews [23]
• there has been much controversy around the exclusion of gabapentin from the NICE guidelines; this was done following an economic analysis showing that the other recommended drugs were a more efficient use of resources; the evidence for efficacy (without an economic analysis) supports the use of gabapentin as a first line agent [1]
• the economic analysis used for the comparison between neuropathic agents commissioned by the HTA Programme was completed but not accepted for publication – the NICE guideline is in the process of being updated in full [1]
• a Cochrane review concluded gabapentin provides pain relief in approximately one third of people who take it for neuropathic pain, with frequent but mostly tolerable adverse effects [24]
• pregabalin [25]:
  • 150-600mg per day has a proven efficacy under chronic neuropathic pain conditions, eg painful diabetic neuropathy, postherpetic neuralgia, and central neuropathic pain
  • may be effective in patients who have previously failed to respond to gabapentin
• a number of antidepressants are effective in treating neuropathic pain [26]:
  • a Cochrane review found at least one third of patients with neuropathic pain who took traditional antidepressants such as amitriptyline obtained moderate pain relief or better
  • there is also evidence that venlafaxine has similar effectiveness to traditional antidepressants
  • approximately one fifth of patients discontinue the therapy due to adverse effects
• approximately one fifth of patients discontinue the therapy due to adverse effects

Pharmacological [1]:
• start amitriptyline 10mg at night:
  • increase gradually to an effective dose or maximum tolerated dose (not above 75mg)
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- consider alternative tricyclic antidepressants such as nortriptyline
  - aim for at least 25mg amitriptyline at night
  - or;
  - start pregabalin 75mg twice a day (a lower starting dose may be appropriate for some people):
    - increase gradually to an effective dose or maximum tolerated dose (no higher than 600mg daily total)
  - aim for at least 150mg twice a day
  - or;
  - start gabapentin 300mg at night:
    - increase gradually first to three times daily and then an effective dose or maximum tolerated dose (no higher than 3.6g daily total)
    - aim for at least 600mg three times a day

- painful diabetic neuropathy:
  - start duloxetine at 60mg per day (a lower starting dose may be appropriate for some people)
  - titrate upwards to an effective dose or the person’s maximum tolerated dose of no higher than 120mg per day

- classical trigeminal neuralgia:
  - consider carbamazepine as first line:
    - starting at 100mg twice a day increasing to an effective dose or maximum tolerated dose (no higher than 1.6g daily total)
  - aim for 200mg four times a day, or 400mg modified release twice a day may be better tolerated
  - oxcarbazepine, baclofen and lamotrigine are alternatives
  - early specialist referral may be appropriate to consider interventions and surgery

NB: The use of amitriptyline, oxcarbazepine, baclofen, and lamotrigine for this indication is outside of their marketing authorisation (product licence) in the UK.

Experts recommend asking the patient to keep a short term diary of response to a drug and how it is taken, because patients often do not adhere to the instructions, or expect a 100% response which is only possible for trigeminal neuralgia. Otherwise the likely improvement is 30-50%. The diary should be discontinued after initial use to prevent too much focus on one aspect of the condition [1].

The dose to aim for is based on expert advice as many patients are often under-treated with a drug when it is deemed to have ‘failed’ [1].

Multidisciplinary (MDT) assessment at early stages can flag up the benefits of non-pharmacological (combined psychological and physical) pain management approaches, eg TENS or acupuncture [18].

NB: For medication contraindications and cautions, consult product information [18].

References:
Please see the care map's Provenance.

13 Topical treatment for focal neuropathies

Quick info:
Localized areas of neuropathic pain may respond to topical lidocaine patches or capsaicin (eg 0.075% cream 3-4 times a day) without the need for systemic therapy – examples are [1]:
- dermatomal post herpetic neuralgia
- a tender area from nerve trauma

A single 60-minute treatment with a capsaicin 8% patch has been found to reduce postherpetic neuralgia for up to 12 weeks, regardless of concomitant systemic neuropathic pain medication use [27].

Adverse effects of capsaicin [28]:
- local skin irritation, which is often mild and transient but may lead to withdrawal, is common
- systemic adverse effects are rare
- estimates of benefit and harm are not robust due to limited data and inconsistent outcome definition

References:
Please see the care map's Provenance.

14 Second-line treatment

Quick info:
Second-line treatment [1]:
- reassessment should be within two weeks until pain is better controlled
- add in or change to another first line drug

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Amitriptyline and either gabapentin or pregabalin may be combined if partially effective [1]:
- if gabapentin or pregabalin have not been effective or limited by side effects, it is reasonable to try the other of the two
- when withdrawing or switching treatment, taper the withdrawal regimen to take account of dosage and any discontinuation symptoms

NB: The use of amitriptyline for this indication is outside of its marketing authorisation (product licence) in the UK.
A Cochrane review concluded that while the superior efficacy of two-drug combinations for neuropathic pain has been demonstrated, it was not possible to recommend any one specific drug combination [29].
Combinations of antidepressants are not generally recommended — however, if a patient is already taking a selective serotonin re-uptake inhibitor (SSRI) or serotonin and noradrenaline re-uptake inhibitor (SNRI) for their mood, some specialists would consider adding in amitriptyline starting at 10mg but not going above 25mg daily [1].

References:
Please see the care map's Provenance.

15 Add in tramadol as third line treatment

Quick info:
Reassessment should be within two weeks until pain is better controlled. The National Institute of Health and Clinical Excellence (NICE) supports the use of tramadol in neuropathic pain [17].
Tramadol should be used with caution in [1]:
- people on selective serotonin re-uptake inhibitor (SSRI) antidepressants, as there is the potential for a serious serotonergic crisis
- vulnerable patients — tramadol can trigger epileptic seizures
- people on high doses of tricyclics

References:
Please see the care map's Provenance.

16 Review if not improved, and consider referral for further specialised diagnostic testing

Quick info:
Review if not improved and consider referral to specialist [1]:
- refer if there is no significant improvement and to clarify the diagnosis [1]
- consider managing on other pathways as clinically indicated, eg for radicular pain see 'Spinal pain' care map [1]
- specialist referral — consider no later than 6 months [1]
- stronger opioids can be considered if the practitioner is competent with long term management of opioids and problems arising [1]:
  - this must include an understanding of equivalent doses [1]
  - please see the British Pain Society's guidelines on long term opioids in non cancer pain [13]

References:
Please see the care map's Provenance.

18 Confirm diagnosis and consider multidisciplinary team (MDT) referral

Quick info:
Specialised tests will be required (eg imaging and nerve conduction studies as appropriate) [1].
Multidisciplinary team (MDT) assessment at early stages can flag up the benefits of non-medical (combined psychological and physical) pain management approaches [18].

References:
Please see the care map's Provenance.

19 Develop and agree a management plan with patient including ongoing assessment

Quick info:
Describe the options for treatment available to allow for patient choice [1]:

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• self-help
• medication
• cognitive behavioral multidisciplinary pain management

There are considerable numbers of studies supporting CBT in chronic pain but very few looking at the subset with neuropathic pain [22].

References:
Please see the care map's Provenance.

20 Consider interventional pain therapies and medications that require specialised supervision

Quick info:
Medications less widely available can be delivered by a variety of routes and may have value in treating the most resistant cases, eg:
• lidocaine [30]
• ketamine [31]
• high dose capsaicin (eg topical 8% patch) [1]
• focal diagnostic or therapeutic injections (eg with corticosteroids or botulinum toxin type A) and other interventional pain therapies [1]

Stronger opioids may have value and need careful management, especially when switching from one to another, eg [1]:
• morphine
• oxycodone
• methadone
• fentanyl
• buprenorphine
• hydromorphone

References:
Please see the care map's Provenance.

21 Provide a multidisciplinary review to consider treatment options

Quick info:
Provide a multidisciplinary review to consider treatment options, including:
• spinal implants [32]
• spinal pathway (see 'Spinal pain' care map) [1]
• intrathecal (IT) drugs [1]
• spinal cord stimulation – recommended as a treatment option for adults with chronic pain of neuropathic origin [32]
• spinal drug delivery – may be appropriate for the most intractable cases [1]
• deep brain stimulation – should only be used in patients with refractory chronic pain syndrome that other treatments have failed to control [33]

Offer group or one-to-one multidisciplinary care [34].

References:
Please see the care map's Provenance.
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