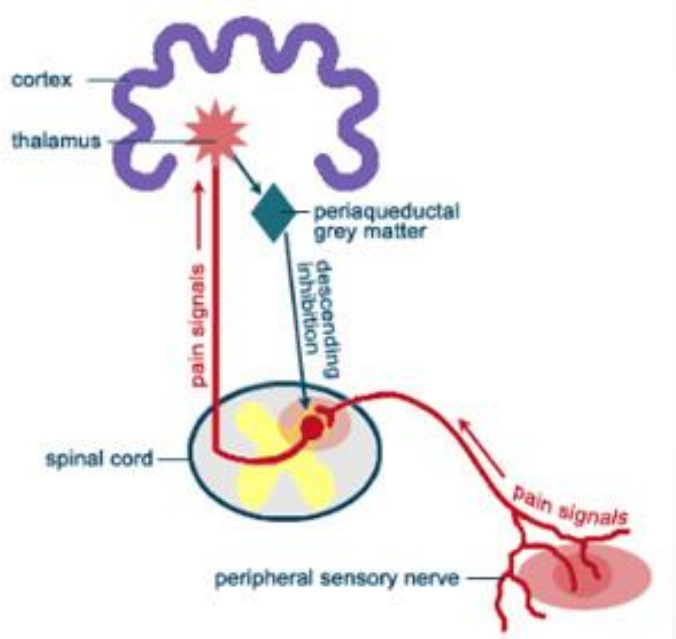
Neuropathic Pain in Palliative Care

Neuropathic Pain in Advanced Cancer

- Affects 40% of patients
- Multiple concurrent pains are common
- Often complex pathophysiology with mixed components
  - Nocioceptive
  - Neuropathic
  - Referred

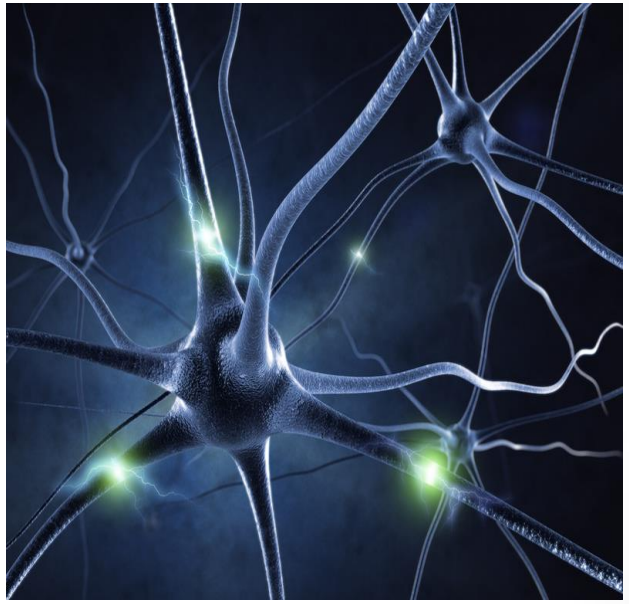


Neuropathic Pain

‘Pain caused by a lesion or disease of the somatosensory nervous system'.

- Central neuropathic pain is caused by a lesion or disease of the central somatosensory nervous system
- Peripheral neuropathic pain is caused by a lesion or disease of the peripheral somatosensory nervous system

IASP 2011

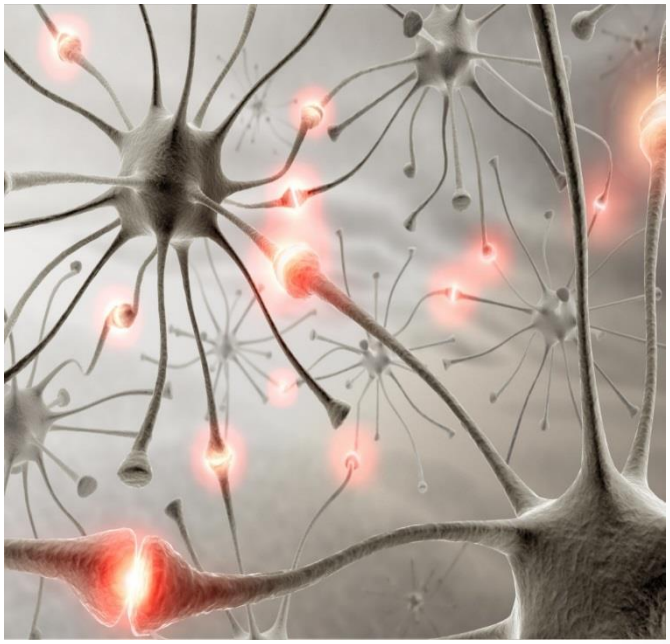


Aetiological Classification

Cause	Examples	Incidence per 100 000 (USA)
Trauma	Post surgery Phantom limb Spinal cord injury Complex regional pain syndrome	? 50% 20 50
Infection/inflammation	Post herpetic neuralgia HIV	180 5
Cancer	Invasion/compression	75
Ischaemia	Painful diabetic neuropathy Central post stroke pain	220 10
Compression	Sciatica Trigeminal neuralgia (Cancer)	775 5
Drugs	Chemotherapy e.g. paclitaxel Reverse transciptase inhibitors	

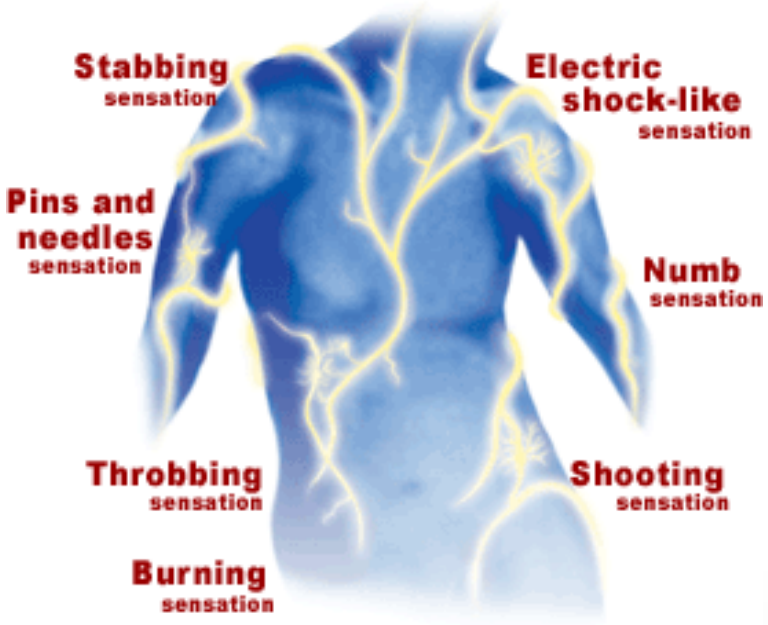
Pathophysiology

- Peripheral
  - Ion channels
  - Neuropeptides
  - Nociceptor sensitisation
  - Abnormal axonal responses
- Central
  - Central sensitisation
  - Cortical re-organisation
  - Spinal re-organisation



Characteristics

- Positive phenomena
  - Characteristics
    - Burning
    - Electric shock
    - Lancinating
  - Sensory disturbance
    - Hyperalgesia
    - Allodynia
    - Hyperpathia



Characteristics

- Negative phenomena
  - Impaired sensation
    e.g. pin-prick
- Autonomic features
  - Vasomotor (blood flow)
  - Sudomotor (sweat glands)
- Greater pain intensity than nocioceptive pain

Principles of pain control

- Determine cause of pain
- Treat cause of pain
- Good analgesia
  - By the clock
  - By the mouth
  - By the ladder
- With this approach around 80% pain can be controlled

Opioids for moderate to severe pain

When morphine doesn't work

- The clinical response to morphine is highly variable
- Less pain relief with single doses of opioids
- More likely to escalate opioid doses
  - Inadequate analgesia
  - Intolerable side effects
- Need to consider
  - Alternative opioids
  - Co-analgesics

Co-analgesic (adjuvant drugs)

- Drugs that have a primary indication other than pain
- Used to enhance the analgesic efficacy of opioids
- Can treat symptoms that exacerbate pain
- Can help patients balance dose related adverse effects of opioids
- Fewer patients experience pain relief from co-analgesics than from opioid analgesics

Co-analgesics

NICE Guidance – First line therapies

- Antidepressant
  - Amitriptyline or Duloxetine
- Anticonvulsant
  - Gabapentin or Pregabalin
- *NB - Duloxetine and pregabalin are only included as first line as they are licenced for this indication and amitriptyline and gabapentin are not*

NICE - Guidance

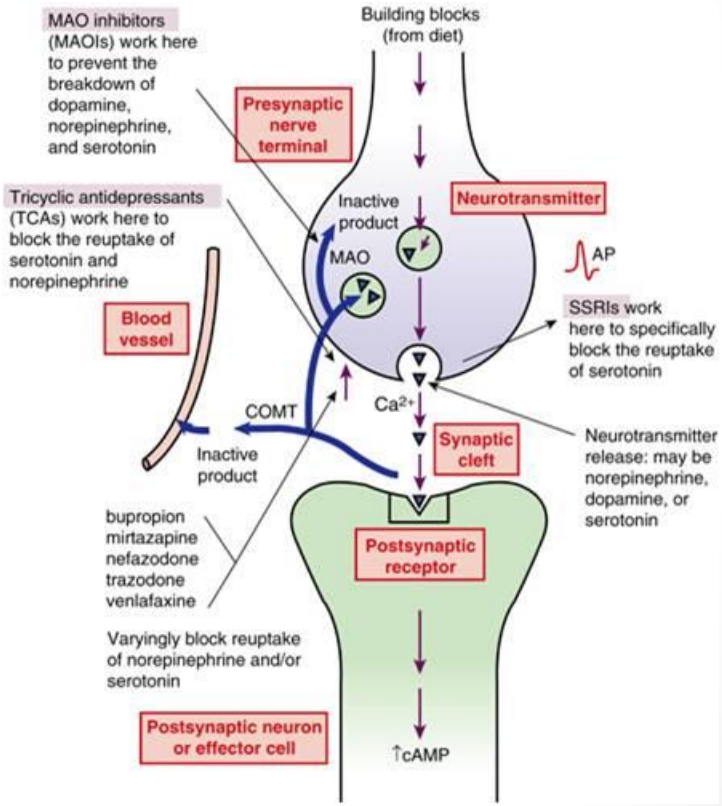
- Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment
- If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated.
- Consider tramadol only if acute rescue therapy is needed *(different issues for patients with mixed nociceptive and neuropathic pain)*
- Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.

Recommendations are based on

- Efficacy and side effect data
  - No significant difference between gabapentin and pregabalin
- Economic data
  - NICE draft guidance reports that both amitriptyline and gabapentin represent good value for money.
  - For duloxetine and pregabalin, mean cost-per-QALY estimates suggest poor value for money in comparison with less expensive treatments, particularly gabapentin and amitriptyline.

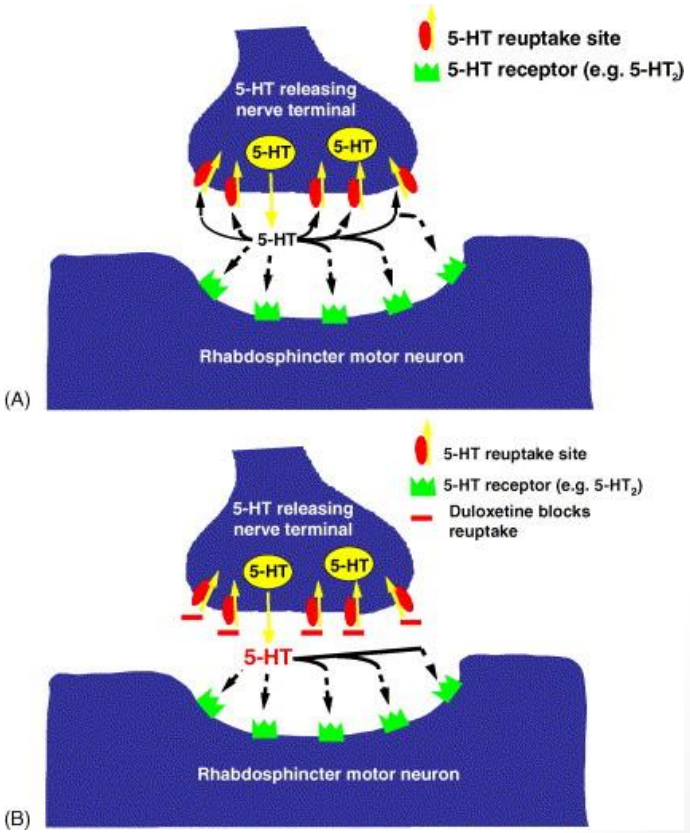
Antidepressants

- TCA e.g. amitriptyline
  - SSRI and NARI
  - Possible NMDA receptor antagonist
- Main analgesic action by potentiation of descending inhibitory pathways
- NNT 2.0
- Analgesic action at lower doses than for depression
- Limited by side effects



Antidepressants

- SNRIs e.g. duloxetine
- Main analgesic action by potentiation of descending inhibitory pathways
- NNT 4-5
- Acts within days
- Analgesia at lower doses than for depression
- Good side effect profile



Anticonvulsants

- Gabapentinoids e.g. gabapentin, pregabalin
- Main action
  - Interacts at the αδ site of calcium channels
  - Inhibits glutamate, NA and substance P release
  - Decreased neurotransmitter release prevents the spread of neuronal excitability
- Maximum action by 2 weeks
- NNT 3.5
- Moderate side effects

NMDA Antagonists

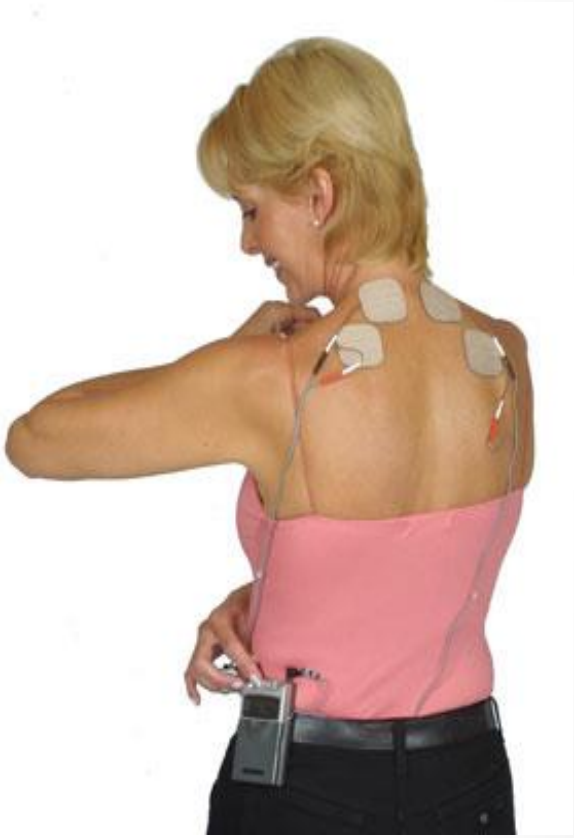
- Ketamine
  - Anaesthetic
  - Opioid sparing effects
  - Clinically useful in nocioceptive and neuropathic pain
  - No NNT data
  - Analgesia at sub-anaesthetic doses
  - Psychomimetic side effects

NMDA Antagonists

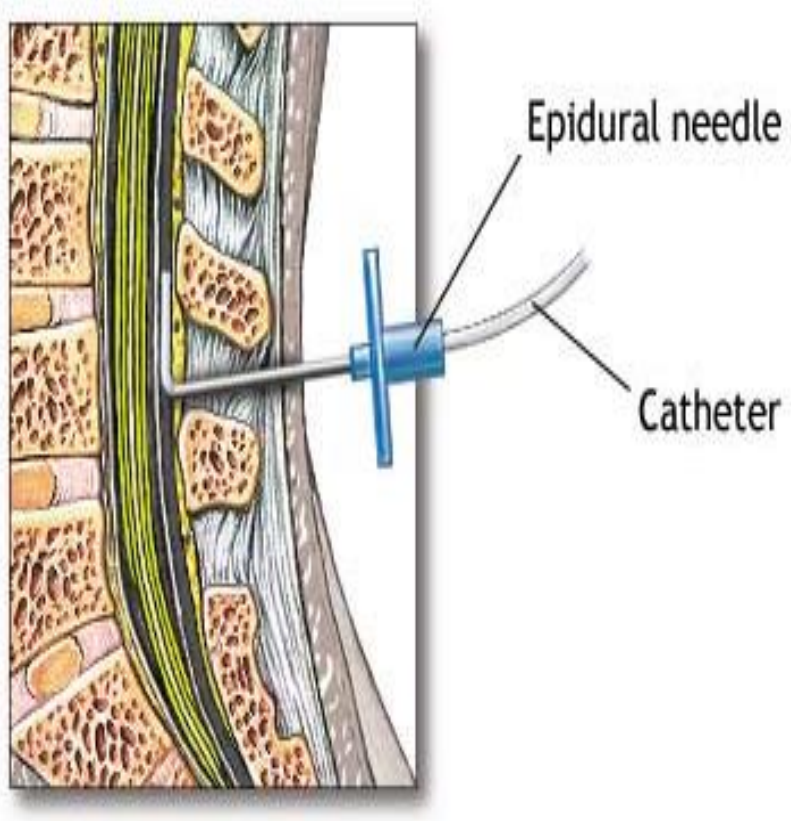
- Methadone
  - Varied receptor properties
    - Primarily a mu agonist with some δ agonist action
    - NMDA antagonist
    - SSRI
  - Lack of known metabolites
  - Long unpredictable half-life can result in accumulation
  - Different titration and initiation process to other opioids
  - Can be used as a co-analgesic as well as an alternative opioid

TENS

- Originally developed as a way of controlling pain through the 'gate' theory.
- When set on low pulse rate may also stimulate endorphin release
- Varying evidence for efficacy (Cochrane review inconclusive)
- Gives patient control
- Usually well tolerated



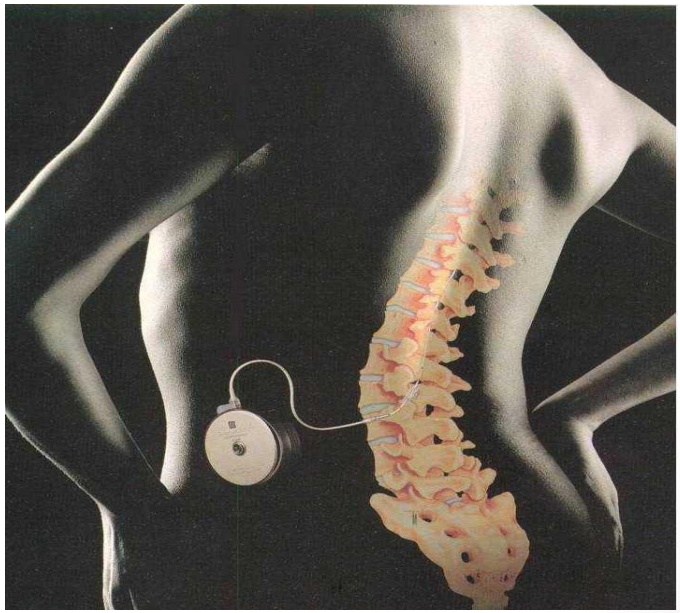
Interventional techniques



- Interventional techniques
  - Modulative
    - Neuraxial procedures
    - Nerve stimulation
      - TENS
  - Ablative
    - Neurolytic blocks

Spinal cord stimulation

- Direct stimulation of the spinal cord
- Blocks pain signals reaching brain
- Concept first utilised in 1967



Summary

- Pain is common in advanced cancer
- The nature of this pain is complex
- Neuropathic pain is more severe and more difficult to control than nocioceptive pain
- Opioids are still the first line drug
- Co-analgesics include numerous drugs and diverse classes
- Sequential trials of adjuvants is needed
- But – always treat the whole patient and not just the pain

Who Ya Gonna Call?

Specialist Palliative Care Advice Line

(North Herts – 01462679540)

PHARMACOLOGICAL MANAGEMENT OF NEUROPATHIC PAIN

STEP ONE - ASSESS & TREAT UNDERLYING CAUSE

STEP TWO - FOLLOW WHO ANALGESIC LADDER

STEP THREE - ADD A NEUROPATHIC ANALGESIC *EITHER* ANTIDEPRESSANT *OR* ANTICONVULSANT

ANTIDEPRESSANTS	ANTICONVULSANTS
1st line Amitriptyline	1st line Gabapentin
2nd line Duloxetine	2nd line Pregabalin

STEP 4 - IF PAIN NOT CONTROLLED AT THERAPEUTIC DOSE ADD A DRUG FROM THE ALTERNATIVE CLASS

STEP 5 - IF PAIN NOT CONTROLLED AT THERAPEUTIC DOSES CONSIDER THIRD LINE ANALGESICS

NMDA ANTAGONISTS	MISCELLANEOUS
Methadone	Lidocaine plasters
Ketamine	Dexamethasone

OTHER INTERVENTIONS, SUCH AS TENS AND NERVE BLOCKS, CAN BE CONSIDERED AT ANY STAGE