

# Final FRCA Teaching

## 1<sup>st</sup> December 2021

**Dr Robin Correa FRCA FFPMRCA MMedEd**  
**Consultant Pain Management**  
**and Anaesthetics**



# Neuropathic Pain and CRPS

- Definition of Pain
- Classification
- Neuropathic Pain
- CRPS

# Pain

## Definition

IASP ( International Association for the Study of Pain)

- An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

# Classification

- Neuropathic Pain (IASP)

Pain caused by a lesion or disease of the somato-sensory system

## Incidence

Neuropathic characteristics seen in 7–8% of adults with pain.

25% of diabetics and 35% of those with HIV have neuropathic pain

- Nociceptive Pain

# Classification

Clinical characteristic	Neuropathic pain	Nociceptive pain
Cause	Injury to the nervous system, often accompanied by maladaptive changes in the nervous system	Damage or potential damage to tissues
Descriptors	Lancinating, shooting, electric-like, stabbing pain	Throbbing, aching, pressure-like pain
Sensory deficits	Common—for example, numbness, tingling, pricking	Uncommon; if present they have a non-dermatomal or non-nerve distribution
Motor deficits	Neurological weakness may be present if a motor nerve is affected; dystonia or spasticity may be associated with central nervous system lesions and sometimes peripheral lesions (such as complex regional pain syndrome)	May have pain induced weakness
Hypersensitivity	Pain often evoked by non-painful (allodynia) or painful (exaggerated response) stimuli	Uncommon except for hypersensitivity in the immediate area of an acute injury
Character	Distal radiation common	Distal radiation less common; proximal radiation more common
Paroxysms	Exacerbations common and unpredictable	Exacerbations less common and often associated with activity

# Causes

- Trauma
- Diabetes
- Trigeminal Neuralgia
- Drugs – Chemotherapy, Amiodarone, Nitrofurantoin, Phenytoin
- Conditions  
Excessive alcohol consumption, infections, chronic liver disease or kidney disease, cancers like lymphoma and multiple myeloma

# Terms

---

**Allodynia:** Painful response to a normally innocuous stimulus

**Central pain:** A subset of neuropathic pain caused by a lesion or disease of the central somatosensory nervous system

**Central sensitization:** Increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold sensory input

**Deafferentation pain:** Pathological pain condition associated with a partial or complete loss of sensory input from a part of the body after lesions in somatosensory pathways, often as a result of reorganization in the central nervous system. Common examples include phantom limb pain and brachial plexopathy

**Descending modulation:** The process by which pathways that descend from the brain to the spinal cord modify incoming somatosensory information so that the perception of and reactions to somatosensory stimuli are altered, resulting in increased or decreased pain

**Ectopic discharge:** Trains of ongoing electrical nerve impulses that occur spontaneously without stimulation or originate at sites other than the normal location (or both). This phenomenon typically occurs after nerve injury

**Ephaptic transmission:** The phenomenon by which two independent nerves communicate with each other through an artificial synapse, which often develops after injury to the insulating myelin sheath that normally prevents crosstalk between parallel nerves

**Hyperalgesia:** Increased pain response to a normally painful stimulus

# Terms

**Neuroplasticity:** Changes in neural pathways and synapses that result from bodily injury or changes in behavior, the environment, or neural processes. This is consistent with the concept that the brain is a dynamic organ that constantly changes in response to internal and outside events throughout life

**Nociception:** The neural responses of encoding and processing noxious stimuli

**Nociceptive pain:** Pain that arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation. Nociceptive pain arises from actual or potential damage to non-neural tissue and can be categorized as visceral or somatic

**Noxious stimulus:** A stimulus that damages or threatens to damage normal tissues

**Peripheral sensitization:** A lowering of the stimulus (pain) threshold for nociceptor activation and an increased frequency of nerve impulse firing in response to stimulation (hyperexcitability). Peripheral sensitization is often found at the site of tissue damage or inflammation

**Sympathetically maintained pain:** Pain that is enhanced or maintained by a functional abnormality of the sympathetic nervous system, such as functional sympathetic afferent coupling or increased expression of adrenergic receptors at the peripheral terminals of nociceptive afferent fibers

**Windup:** Progressive increase in the frequency and magnitude of firing of dorsal horn neurons produced by repetitive activation of C fibers above a critical threshold, leading to a perceived increase in pain intensity



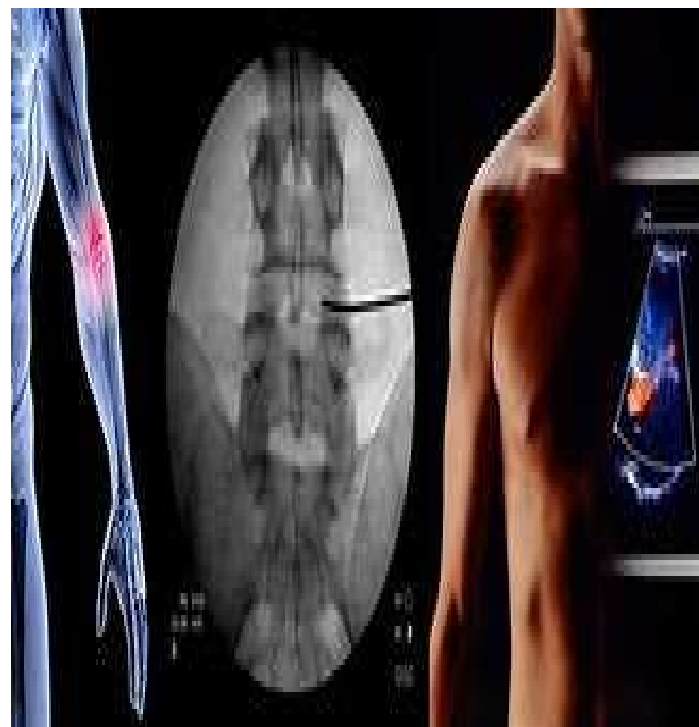
# Management

## **Interventional modalities**

- Local nerve blocks
- Spinal or epidural steroids
- Neuroablation
- Neuromodulation
- Neurosurgical procedures

## **Medications**

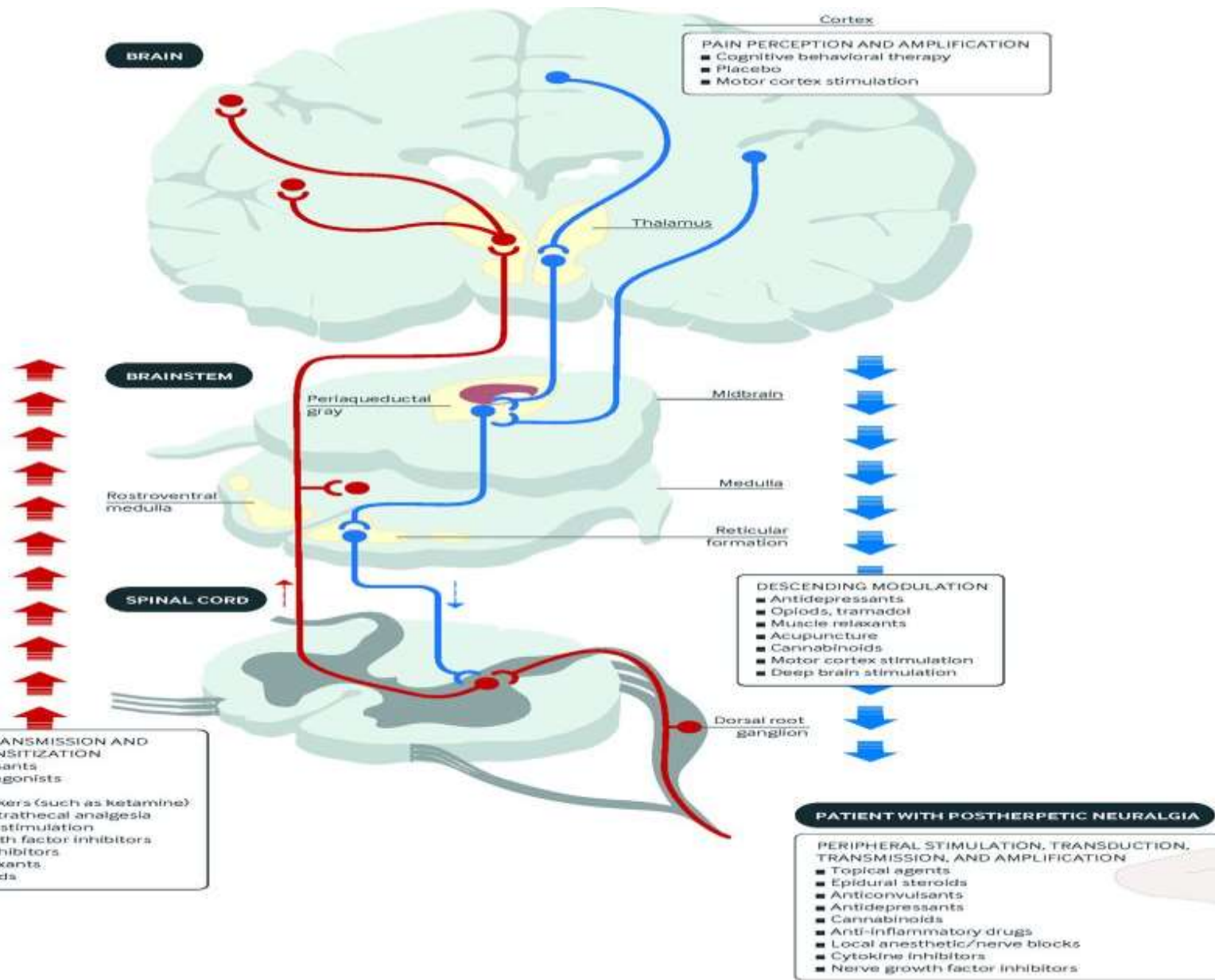
# Neuroablation



# Neuromodulation



# Medications



- SYNAPTIC TRANSMISSION AND CENTRAL SENSITIZATION**
- Anticonvulsants
  - Adrenergic agonists
  - Opioids
  - NMDA blockers (such as ketamine)
  - Epidural/intrathecal analgesia
  - Spinal cord stimulation
  - Nerve growth factor inhibitors
  - Cytokine inhibitors
  - Muscle relaxants
  - Cannabinoids

- PAIN PERCEPTION AND AMPLIFICATION**
- Cognitive behavioral therapy
  - Placebo
  - Motor cortex stimulation

- DESCENDING MODULATION**
- Antidepressants
  - Opioids, tramadol
  - Muscle relaxants
  - Acupuncture
  - Cannabinoids
  - Motor cortex stimulation
  - Deep brain stimulation

- PATIENT WITH POSTHERPETIC NEURALGIA**
- PERIPHERAL STIMULATION, TRANSDUCTION, TRANSMISSION, AND AMPLIFICATION**
- Topical agents
  - Epidural steroids
  - Anticonvulsants
  - Antidepressants
  - Cannabinoids
  - Anti-inflammatory drugs
  - Local anesthetic/nerve blocks
  - Cytokine inhibitors
  - Nerve growth factor inhibitors

# Medications

NICE Guidelines

[Neuropathic pain in adults: pharmacological management in non-specialist settings](#) (2013 updated 2020) NICE guideline CG173

# NICE guideline CG173

## Treatment



### All neuropathic pain (except trigeminal neuralgia)

For advice on treating sciatica, see the NICE guideline on low back pain and sciatica. Also see the September 2020 update information.

- Offer a choice of amitriptyline, duloxetine, gabapentin, or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia)[C],[D]
- If the initial treatment is not effective or is not tolerated, offer one of the remaining three 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 (see below about long-term use)
- Consider capsaicin cream[E] for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments

# NICE guideline CG173

## Treatments that should not be used

- Do not start the following to treat neuropathic pain in non-specialist settings, unless advised by a specialist to do so:
  - cannabis sativa extract
  - capsaicin patch
  - lacosamide
  - lamotrigine
  - levetiracetam
  - morphine
  - oxcarbazepine
  - topiramate
  - tramadol (this is referring to long-term use; see above for short-term use)
  - venlafaxine
  - sodium valproate (follow MHRA safety advice on sodium valproate)

# Neuropathic Pain





# CRPS

## Father of teacher, 27, with a chronic pain condition dubbed 'suicide disease' because of how many sufferers take their lives says sharing her journey on TikTok has given her 'purpose and a reason to go on'

- Amy Pohl, now 28, a former primary school teacher of Rugby, Warwickshire, was diagnosed with complex regional pain syndrome (CRPS) in January 2018
- It's often dubbed suicide disease because of how many sufferers take their lives
- Amy has spent her life in specialist care and rehabilitation facilities ever since
- Covid-19 created 'physical and psychological barrier' between her and family
- After joining TikTok 'for a joke', her inspiring videos that capture her fight with CRPS, FND and her rehab story have seen her amass 1 million followers

By HAYLEY RICHARDSON FOR MAILONLINE

PUBLISHED: 16:06, 12 August 2021 | UPDATED: 16:06, 12 August 2021



The father of a woman battling 'suicide disease' which left her bedridden and in agony has told how joining **TikTok** has given her 'sense of purpose' and helped her stay connected to the world during the pandemic.



# CRPS

- Background
- Classification
- Pathophysiology
- Diagnosis Criteria
- Treatment

# Background

- CRPS Complex Regional Pain Syndrome
- Previously known as

Reflex Sympathetic Dystrophy

Causalgia

Algoneurodystrophy

Sudeck atrophy

- Incidence 0.07%\*

\* *Elsharydah et al. Pain Physician 2017; 20(2): E257-68*

# Background

Most common primary causes \*:

- Fractures - 42%
- Blunt trauma without fractures (sprains) – 21%
- Surgery – 12%
- Carpal Tunnel Syndrome – 7%
- No clear precipitating event – 7%

\* *Ott S, Maihofner C. Journal of Pain 2018;19(6):599-611*

# Classification

## Comparison of CRPS Types

Signs and symptoms	CRPS Type I	CRPS Type II
Precipitating event	Sometimes	Yes
Single Peripheral nerve involvement	No	Yes
Physiological change in affected limb	Yes	No
Cardinal signs	<ul style="list-style-type: none"><li>• Spontaneous pain</li><li>• Swelling</li><li>• Different skin temperatures</li></ul>	<ul style="list-style-type: none"><li>• Burning pain</li><li>• Allodynia</li><li>• Hyperalgesia</li></ul>
Progressive	Yes	Sometimes
Bone atrophy	Yes	No

# Classification

Stages	Symptoms	Time Frame
<b>Acute stage</b>	<ul style="list-style-type: none"><li>▶ Affected limb swollen, red, burning</li><li>▶ Increased diaphoresis of affected limb</li><li>▶ All symptoms are near the site of original injury</li></ul>	Within weeks of injury
<b>Dystrophic stage</b>	<ul style="list-style-type: none"><li>▶ Skin of limb is cool and diaphoretic</li><li>▶ Sudek's atrophy of bone on X-ray</li><li>▶ Pain occurs throughout limb, not just at site of injury</li></ul>	Within months of injury
<b>Atrophic stage</b>	<ul style="list-style-type: none"><li>▶ Skin becomes pale and shiny</li><li>▶ Atrophy of muscle and bone in the affected limb</li><li>▶ Pain may be constant even with treatment</li></ul>	For years after injury

# Pathophysiology

- Inflammation
- Autonomic Nervous System Dysfunction
- Autoimmunity

# Pathophysiology

## Inflammation

- Immune system activation with release of pro-inflammatory cytokines (e.g. IL-6) → Histamine induced vasodilatation → redness, swelling, warmth of acute phase
- Cytokine induced osteoclast and osteoblast activity → rapid bone turnover and osteoporosis of chronic phase



# Pathophysiology



# Pathophysiology

## **Autonomic Nervous System Dysfunction**

- Lower sympathetic activity in acute phase with up-regulation of  $\alpha$  – adrenergic receptors leading to vasodilatation
- Chronic phase characterised by endothelin -1 mediated vasoconstriction leading to a cold, blue, clammy limb

## **Autoimmunity**

- Elevated auto-antibodies seen in the serum, skin and tissues
- Produce pain by sensitising nociceptors

# Diagnostic Criteria



# Budapest Criteria

Clinical Diagnostic Criteria (Budapest Criteria) for Complex Regional Pain Syndrome				
	A - D must apply for a confirmed diagnosis of CRPS			Y/N
<b>A</b>	Continuing pain, which is disproportionate to any inciting event.			
<b>B</b>	The Patient must report at least one <i>symptom</i> in <i>three</i> of the <i>four</i> following categories:			
	<b>Categories</b>	<b>Description</b>	<b>Y/N</b>	
	Sensory	Reports of hyperesthesia and/or allodynia		
	Vasomotor	Reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry		
	Sudomotor/ Oedema	Reports of oedema and/or sweating changes and/or sweating asymmetry		
	Motor/ Trophic	Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)		
<b>C</b>	The clinician must observe at least one <i>sign</i> * at the time of the evaluation in <i>two</i> or <i>more</i> of the following categories:			
	<b>Categories</b>	<b>Description</b>	<b>Y/N</b>	
	Sensory	Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)		
	Vasomotor	Evidence of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry		
	Sudomotor/ Oedema	Evidence of oedema and/or sweating changes and/or sweating asymmetry		
	Motor/ Trophic	Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)		
<b>D</b>	There is no other diagnosis that better explains the signs and symptoms.			
* A sign is counted only if it is observed at time of diagnosis				
For research diagnostic criteria the patient must report at least one symptom in each of the 4 categories in part B				

# Treatment

- Physical and Occupational Therapy
- Medications
- Interventions
- Others

# Treatment

## Medications

- Gabapentin
- Biphosphonates
- Vitamin C
- Ketamine
- Oral Prednisolone
- Naltroxone
- Botulinum toxin A (BTX-A)

# Treatment

## Interventions

- Sympathetic blocks
- Spinal Cord Stimulator (SCS)
- Peripheral Nerve Stimulator (PNS)
- Transcranial Magnetic Stimulation
- Amputation

# Treatment

## Others

- Plasma Exchange Therapy
- Mycophenolate
- PDRN ( polydeoxyribonucleotide)



# Reference

Complex Regional Pain Syndrome: A Comprehensive Review

*Taylor SS, Noor N, Urits I et al. Pain Therapy (2021) 10:875- 892*

