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Chronic Regional Pain Syndrome: Emerging Insights and Established Concepts

INTRODUCTION

Complex Regional Pain Syndrome (CRPS) is a chronic and debilitating pain condition primarily affecting the limbs. It is characterized by hyperalgesia (increased sensitivity to pain) and allodynia (pain from non-painful stimuli), often accompanied by sensory, autonomic, motor, and trophic abnormalities. CRPS commonly follows extremity trauma or surgery but remains underreported due to diagnostic challenges and lack of awareness. Misdiagnosis with neuropathic pain syndromes often delays treatment. The introduction of the Budapest Criteria in 2003 has significantly improved diagnostic clarity and remains the gold standard for CRPS diagnosis globally. Patient education plays a crucial role in early identification, adherence to treatment plans, and coping strategies. Empowering patients with knowledge about CRPS may improve outcomes and reduce fear-avoidance behaviours.

DEFINITION AND DIAGNOSTIC CRITERIA

CRPS is classified into two types:
CRPS I: Occurs without identifiable major nerve damage.
CRPS II: Occurs with identifiable major nerve damage.

The Budapest Criteria outlines diagnostic features:

- Continuous pain disproportionate to the inciting event.
- At least one symptom in three of four categories:
  - **Sensory:** Allodynia or hyperalgesia.
  - **Motor/Trophic:** Reduced movement or motor dysfunction.
  - **Sudomotor:** Oedema or altered sweating.
  - **Vasomotor:** Skin colour or temperature asymmetry.
- At least one sign at the time of evaluation in two or more of the same categories.
- Symptoms are not better explained by other diagnoses.

Additional tools such as thermography or skin biopsy may enhance diagnostic accuracy in equivocal cases.

Differential diagnoses include peripheral neuropathies, inflammatory arthritis, vascular disorders, and somatoform pain disorders. A careful clinical assessment is essential to avoid misdiagnosis and inappropriate treatment.

RISK FACTORS

CRPS is more prevalent in women and is often triggered by trauma, fractures, or surgery. Associated conditions include fibromyalgia and carpal tunnel syndrome, although its overall prevalence remains low. Emerging risk factors include smoking, psychological factors such as anxiety or depression, and certain genetic predispositions (e.g. alterations in the HLA gene complex located on chromosome 6).

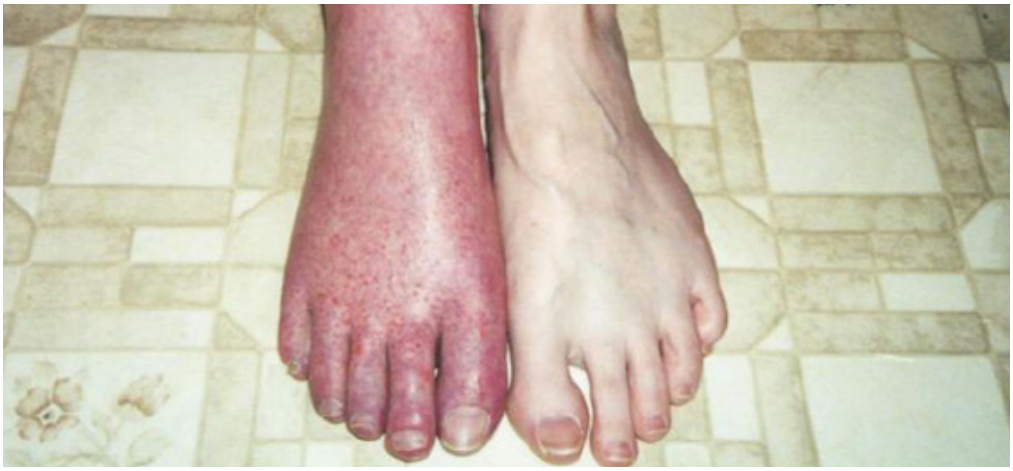
PATHOPHYSIOLOGY

The mechanisms underlying CRPS are multifactorial and involve:

- **Peripheral Nervous System:** Early injury leads to nociceptive sensitisation and release of pro-inflammatory mediators, lowering pain thresholds.
- **Central Nervous System:** Persistent nerve stimulation enhances synaptic activity in the dorsal horn, amplifying pain perception.
- **Autonomic Dysregulation:** Acute phases involve decreased norepinephrine levels, causing warmth and swelling, which later shift to cold, cyanotic limbs due to catecholamine changes.
- **Autoimmune Factors:** Elevated neuropeptides may trigger inflammatory responses, prolonging inflammation and delaying healing.
- **Genetics:** Alterations in the HLA gene complex may predispose individuals to CRPS-related fixed dystonia.

Emerging research suggests a potential role for mitochondrial dysfunction and oxidative stress in CRPS pathophysiology.

Figure 1.
Image of patient with lower extremity CRPS.



DIAGNOSIS

The diagnosis of CRPS relies on clinical evaluation based on history, examination, and exclusion of alternative diagnoses:

- **History:** Patients typically present with pain disproportionate to trauma in a non-dermatomal distribution.
- **Physical examination:** Comparison of the affected and unaffected limbs for sensory, vasomotor, sudomotor, and motor/trophic abnormalities as outlined by the Budapest Criteria.
- **Investigations:** Blood tests, imaging (e.g. bone scintigraphy, thermography) and nerve conduction studies help rule out alternative diagnoses.

Practical tools such as validated questionnaires and pain scales (e.g. McGill pain questionnaire) can assist in assessing severity and monitoring treatment response.

MANAGEMENT OPTIONS

CRPS treatment in Malta follows global best practices and incorporates conservative, pharmacological, and interventional approaches:

- **Conservative therapies:** Physical therapy, mirror therapy, acupuncture, and TENS are first-line interventions. Graded motor imagery has shown promise in the early stages of CRPS.
- **Pharmacological treatments:**
  - **Analgesics:** NSAIDs, opioids.
  - **Neuropathic pain medications:** Gabapentin, amitriptyline.
  - **Corticosteroids:** For short-term relief of inflammation.
  - **Topical agents:** Anaesthetic (lidocaine and prilocaine) as well as ketamine creams to reduce allodynia and hyperalgesia.
  - **Sympathetic blockers:** Clonidine.
  - **Bisphosphonates and low-dose naltrexone** are emerging therapies with encouraging results.
- **Interventional techniques:** Sympathetic plexus blocks e.g. stellate ganglion blocks and spinal cord stimulation (SCS). Dorsal root ganglion stimulation (DRG-S) offers targeted pain relief and is being evaluated as a potential standard of care for refractory CRPS.

DISCUSSION

The management of CRPS remains challenging due to its complex and multifactorial pathophysiology, necessitating a multidisciplinary and patient-centred approach. While several treatment modalities show promise, variability in patient response highlights the need for individualized care plans and ongoing research.

Prognosis varies considerably. Early diagnosis and prompt intervention are associated with better outcomes. However, a subset of patients may experience persistent symptoms and disability despite treatment. Long-term follow-up and functional rehabilitation remain essential components of care.

CONCLUSION

Timely diagnosis and comprehensive management strategies are critical for improving outcomes for CRPS patients. Collaborative efforts, both locally and internationally, are essential to enhance access to emerging therapies and optimize care delivery.

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