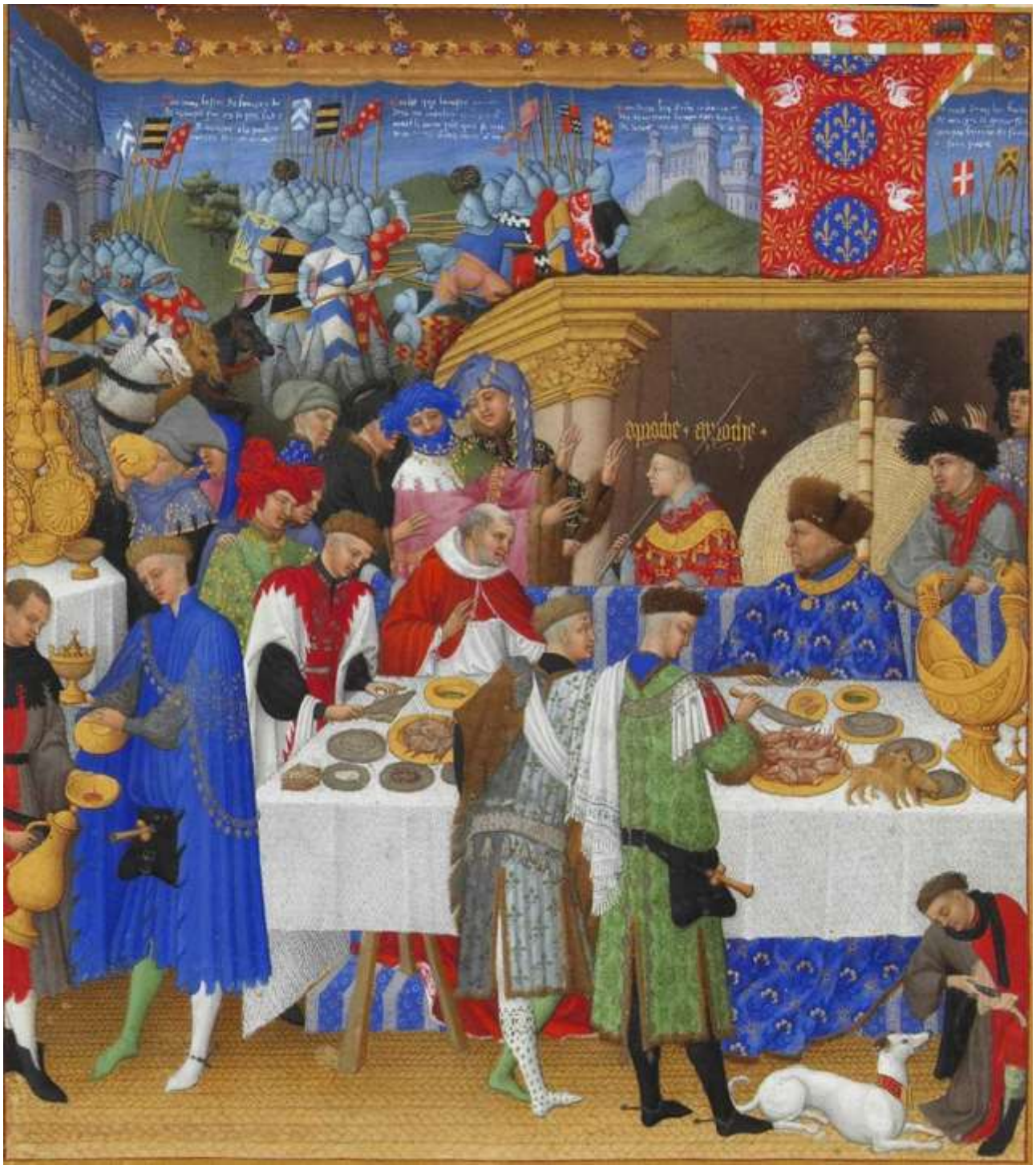
THE NORTHERN HOSPITAL

COMPLEX REGIONAL PAIN SYNDROME



Très Riches Heures du duc de Berry Folio 1, verso: January, (Detail), French Gothic illuminated manuscript on vellum, Herman, Paul, and Johan Limbourg c. 1412-16.

1. *As the Philosopher says at the beginning of the Metaphysics, all men naturally desire to posses knowledge. This can, and should, be traced to the fact that every being has a drive inherent in its own nature directing it towards its own perfection. Since knowledge is the highest perfection of our soul, in which our supreme happiness is found, we are all by our very nature driven by the desire to attain this.*

2. *Many, however, are deprived of this most noble perfection by various causes, both internal and external to man, which preclude his possessing knowledge.*

3. *There are two possible deficiencies or hindrances internal to man, one pertaining to his body, the other to his soul. The one pertaining to his body occurs when his bodily organs are improperly formed, leaving him incapable of receiving impressions through them, as happens with deaf-mutes and the like. The one pertaining to his soul occurs when the soul is dominated by evil through making itself a devotee of harmful pleasures; these bring such disillusionment that the soul, on account of its experience with them, holds everything to be worthless.*

4. *Likewise two causes external to man can be specified, one resulting in unavoidable constraint, the other in laziness. The first is family and civic responsibilities, which quite properly absorb the energies of the majority of men, with the result that they cannot find the leisure required for cultivating the mind. The other is a deficiency in the place where a person is born and raised: this is sometimes such that it not only lacks any institute of higher learning, but is even remote from the company of learned people.*

5. *Two of these causes, the first in each of the above pairs, do not merit censure, and deserve rather to be excused and pardoned. The other two, though in different measure, do deserve blame and abhorrence.*

6. *Anyone who reflects on this can clearly see that there are only a few people who can attain what all desire to possess, and that those who are hindered from so doing, and pass their entire lives starved of this food, are almost beyond number.*

7. *Blessed indeed are those few who sit at the table where they feed on the bread of angels! And pitiful are those who share the food of sheep!*

Dante Alighieri, opening lines of the "Convivio"; c.1304-1307.

By the Thirteenth century Latin remained the lingua franca of emerging nations, but it was no longer the language of the common people. The great medieval Poet, Dante Alighieri revolutionized literature in the Thirteenth century by writing not in Latin which could only be understood by a handful of the highly educated elite, but in the Italian vernacular. In his famous treatise "Convivio" (The Banquet) criticizing the nobility for their lost ideals, he wrote to the general "masses" - in Italian so that he could reach a far wider readership - though of course this readership was still greatly restricted by modern standards, as few could even read at all, let alone read Latin. Nonetheless he set the precedent of writing in the vernacular, and so paved the way for Johannes Gutenberg

in the Fifteenth century, whose printing presses would revolutionize the dissemination of information to the people on a scale unimaginable before, and not equalled until the Victorian telegraph, the wireless of Marconi and the Internet of the late Twentieth century.

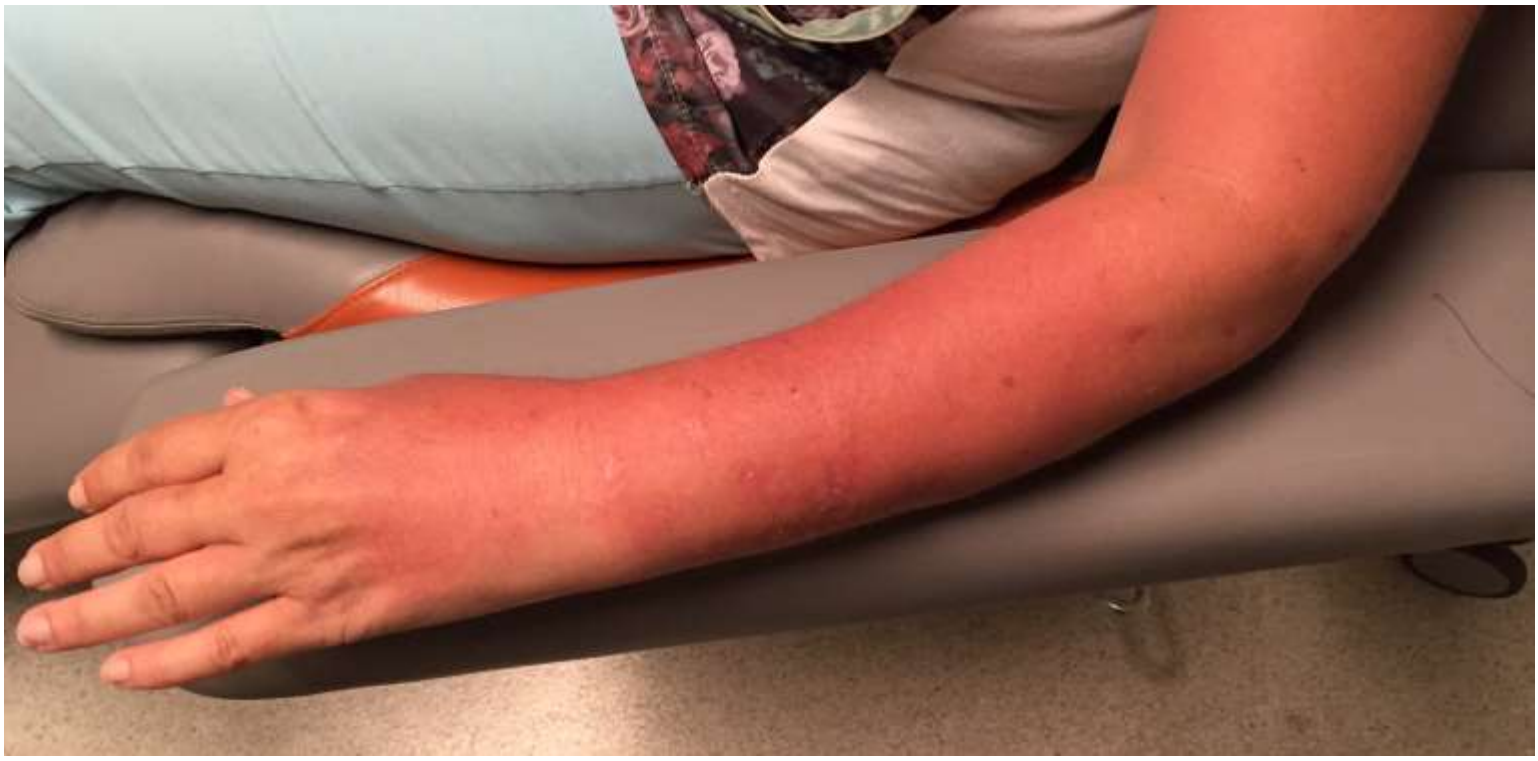
Thirteenth century Florence was a city state wracked with internecine violent partisan politics. Dante felt that the nobility of his time had completely lost touch with the ideals of their privileged station in life. He became utterly disillusioned by the greed and all consuming monetary and self-interest he witnessed within this class. Indeed he himself would become a victim of the factional self-interests that tore his beloved city apart. He would be exiled for political reasons in 1302, and would never set foot in Florence again. But in exile he would become Florence's greatest and most famous citizen. He wrote the "Convivio", in the vernacular Italian, to reach the people not only of Florence but of all Italy. It was an impassioned appeal to the nobility to abandon their self-serving ways and to seek higher learning and knowledge in the arts of philosophy linguistics, the sciences, and history in order to create a better and more truly "noble" society for all. The Convivio is primarily addressed to a well defined class, whom he seeks to educate, "to princes, barons, knights, and many other noble folk, not just men but women who are many in this language, who only know the vernacular and are not learned", (Conviv IX 5). In other words Dante will communicate in a language that all can understand! He invites his readers to a feast where the food served will be knowledge. It is an open invitation to all who hunger for knowledge and a more noble way of life. His readers will sit at his "table" and partake of a great "Banquet".

But despite Dante's best exertions, his work did nothing to halt the internecine self-serving violence and vendetta which was destroying his city. He would reject all factions and become his own party - a party of one. Abandoning his attempts at "education" he would instead vent his anger, despair and frustration through his greatest work - indeed one of the greatest in all of western literature - "The Divine Comedy" which told of the terrifying fate in afterlife that awaited those who strayed from the "true path". He had no hesitation in casting the rich and the powerful, even Popes into the fires of Hell. It was a horrifying vision, and a deeply shocking one to the profoundly religious medieval mind.

Today, Florence, the city that once exiled and condemned Dante to be burnt at the stake, reveres him as its greatest citizen. Many of the grand personages who had held political or personal grudges against Dante would have been long forgotten by history, but by dint of the Divine Comedy, also achieved immortality - as damned souls in the Inferno!

An uncommon and unusual condition exists that presents itself as a potentially disastrous consequence of injury and immobilization of a limb. This condition, already obscure, was long shrouded in its learned but uninformative names. It was once known as "Sudeck's Atrophy", but then became known as "Reflex Sympathetic Dystrophy". Mercifully today it goes by the much more informative and much more vernacular designation of "Complex Regional Pain Syndrome" - a term that the immortal Dante Alighieri himself would most certainly have approved of.

COMPLEX REGIONAL PAIN SYNDROME



A 45 year old woman with, Complex Regional Pain Syndrome (photograph courtesy Dr Peter Kas, Resus.com). This shows the early,"hot florid phase" of the complex regional pain syndrome . The limb is edematous, erythematous and painful. This woman sustained a forearm fracture. Her forearm had been immobilized in a plaster cast for a period of six weeks. One week after removal of her plaster, she developed the features seen and described above.

Introduction

Complex Regional Pain Syndrome (formerly known as **reflex sympathetic dystrophy** and formerly to that, **Sudeck's atrophy**) is an uncommon chronic neuropathic limb pain condition of unknown causation.

In the formerly called complex regional pain syndrome type II where there was a history of nerve injury the condition was referred to as "**causalgia**".

It is associated with abnormalities in:

1. Skin
2. Bone
3. Peripheral nervous system including:
    - Autonomic nerves.

- Sensory nerves.
- Motor nerves.

The diagnosis is currently a clinical one.

The clinical course is variable.

There is little evidence to guide therapy, but combinations of pharmacotherapy, physiotherapies and psychological therapies are used.

Epidemiology [1]

Complex regional pain syndrome accounts for approximately 2 - 5 % of adult and up to 20% of paediatric **pain clinic patients.**

The prevalence in Australia is unknown.

It affects females more, in a 3.5:1 ratio in adults and 9:1 in children.

The prevalence is highest in Caucasians.

Pathophysiology

The condition can be thought of as:

1. Primary:
    - Spontaneous onset of unknown causation
2. Secondary:
    - Triggered by injury, such as a strain or sprain, a distal fracture or surgery, particularly in association with a period of immobilization (splinting/casting)

The pathophysiology of complex regional pain syndrome is uncertain and there are possibly multiple mechanisms.

Suggestions have included inflammatory changes occurring within the CNS as well as the peripheral sympathetic nervous system.

Research using functional imaging and electroencephalogram mapping is providing more information, with demonstrated topographical shrinkage in cortical activation, for example of the hand region of the motor cortex, and reduction in the size of the somatosensory homunculus (reduced face to hand distance).

Altered neurological processing also occurs with the development of:

- Neglect
- Spatial perception changes
- Reduced two-point discrimination.

Clinical features

Important points of history:

1. There may be a history of a traumatic triggering event:
    - Limb trauma
    - Limb surgery
    - Immobilization (splinting/casting)
2. Pain:
    - Pain is usually out of proportion to any preceding injury.
    - The clinical course varies but pain can spread regionally, beyond a single dermatome, for example from hand to forearm.
    - Pain is **neuropathic** in *nature*, i.e it is commonly described as burning, shooting or sharp.
3. Sensory perception disturbances:

    Manifestations can include neuropathic type symptoms such as:

    - Allodynia:
        - ♥ This is pain being sensed with a non-painful stimulus.
    - Hyperalgesia:
        - ♥ This is increased pain being sensed that is out of proportion to a mildly painful stimulus.
    - Hyperaesthesia:
        - ♥ This is increased sensitivity felt with a stimulus. Patients may be unable to tolerate clothes, bedding, wind or water touching their affected limb.

4. Anatomical distribution:

- The syndrome primarily involves the limbs:

  - ♥ The upper limb is affected more in adults

  - ♥ The lower limb is affected more in children.

5. Sleep disturbance is common.

6. Avoidance of using the limb is common.

Important points of examination:

1. Labile autonomic phenomena:

   Changes in skin colour and temperature are seen:

   - A "hot florid" phase of variable duration usually occurs early with a red, warm, sweaty limb.

   - This can later progress to a "blue cold" or "atrophic" phase but some patients have this blue cold phase from the outset.

2 Trophic skin changes:

   - Skin, hair and nail changes can be seen

3. Edema:

   - Swelling can occur in both phases and can fluctuates from mild to extreme.

4. Motor abnormalities:

   Manifestations can vary and may include:

   - Stiffness

   - Impaired coordination.

   - Tremor

   - Weakness

   - A few develop a wasted, contractured, shiny limb.

Diagnostic criteria:

The diagnosis remains a clinical one.

Diagnostic features include symptoms and signs that have no other cause, in several categories (as described above), i.e:

- Sensory
- Vasomotor
- Sudomotor (i.e oedema, sweating)
- Motor
- Trophic skin changes

Depression can also a significant complication in chronic cases

Natural history:

The natural history of complex regional pain syndrome is **variable.**

Some patients' symptoms spontaneously resolve in **weeks** or **months**, while other patients have **persistent** pain and allodynia with stiffness.

A few develop a wasted, contractured, shiny limb.

The prognosis in children is relatively better, as more patients achieve full recovery.

Relapses and spread to other limbs can occur.

Disease progress can be described in general terms as having 3 stages:

Acute Stage:

- The acute stage lasts approximately 3 months and is marked by burning pain, redness and swelling.

Intermediate stage:

- If the condition doesn't respond to treatment or treatment is not initiated, then it may progress to the second stage, where there is swelling, constant pain, with progressive loss of function.

Chronic stage:

- It takes about one year for the process to enter the chronic phase. This involves loss of function and stiffness of the limb, with fibrosis around the joints, which may progress to a claw hand.

Investigations

The diagnosis is clinical.

Investigations are only performed to exclude other diagnoses such as:

- Infection
- Non-union/ malunion
- Missed bony or soft tissue injury.

Management

There is little evidence to guide therapy because of the difficulties in studying specific interventions in complex regional pain syndrome.

These difficulties include the need for multidisciplinary treatments, limited numbers of patients, differing diagnostic criteria, the varying nature and duration of the clinical manifestations, and knowing whether recovery is due to treatment or spontaneous remission.

Treatments are often based on expert opinion and what works in other neuropathic pain conditions.

It is difficult to prepare guidelines or advice for treatment because of the limited number of trials.

One approach is a mixture of several drugs and other interventions according to the symptomatology and comorbidities present.

Having an agreed treatment plan can help with management.

Pharmacotherapy:

The goal of pharmacotherapy is to assist functional improvement.

Options include:

1. Simple analgesics:

   The early phase may be managed with simple analgesics such as:

   - **Aspirin**

- **Paracetamol**
- **NSAIDs**

Although these agents can assist with pain control they do not alter the overall course of the disease.

2. Opioids:

The ongoing use of **opioids** for complex regional pain syndrome is controversial. In general they are best avoided due to significant dependence, tolerance and abuse potential when given for a **chronic** condition.

Tramadol and **tapentadol** may be better options than the pure opioids due to their additional modality of action (anti-neuropathic) and lesser potential for addiction and abuse.

3. Corticosteroids:

Corticosteroids may be considered in the **early inflammatory phase**, however, the optimal time for commencing these is uncertain.

A **prednisolone** dose of 30 mg/day can be gradually tapered off, but there is no evidence for any particular regimen.

4. Anti-neuropathic drugs:

Some antiepileptic drugs have anti-neuropathic effects.

These are probably the best agents to use, at least on theoretical grounds.

Options include:

- **Gabapentin**
- **Pregabalin**
- **Carbamazepine**

5. Antidepressants:

These may be required for significant depression, but the potential for interaction with concurrent agents such as tramadol and the precipitation of **serotonin syndrome**, must be kept in mind.

6. Other agents:

A large host of alternative agents have been put forward, but without a good evidence base for them.

The widely disparate mechanisms of action of these agents, probably reflect a relative lack of efficacy for any given one of them.

7. Sympathetic nerve blockade:

Sympathetic blockade (in the form of **stellate ganglion block** and **lumbar sympathetic block**) has been used extensively despite limited supporting evidence.

The blocks are generally offered for:

- The acute hot florid phase
- The blue cold phase, if there is prominent associated oedema.

It is unclear whether permanent sympathectomy is better than repeated temporary local anaesthetic blocks.

Epidural block (providing **sympathetic and somatic** block) is also sometimes used.

Physiotherapy:

The emphasis is on graded rehabilitation and movement of the limb with physiotherapy and occupational therapy.

The patient must move, exercise and reintegrate the limb into normal everyday activity.

Physiotherapists and occupational therapists have a key role.

Treatment regimens include:

- Desensitization contrast baths (ice-cold vs hot-warm water immersion)
- Hydrotherapy
- Graded exercise/ strengthening, gradual increase in weight loading of the limb (by using weights, or pushing down on a set of bathroom scales)
- Sensory re-education/exposure therapy (placing limb in sand, use of tactile gloves and texture boxes)
- Edema control (compressive garments).
- Graded motor imagery also has some evidence supporting its use.

- This involves phased “brain retraining” with left- right (laterality) discrimination training (photographs and mobile apps to identify limb side, improving accuracy and speed of response), proceeding to imagined and then mirrored movements.

- Transcutaneous electrical stimulation has also been used but without an evidence base to support it.

Psychotherapy:

Psychological therapies should be offered if a patient is making no or slow progress in the acute phase, and to all patients in the chronic phase as depression can occur.
Ongoing pain, physical, emotional and social losses can lead to significant psychological problems including:

- Depression

- Anxiety

- Fear of movement and fear of harm/re-injury

Patient education about the pathophysiology, the negative effects of disuse and the reasons for resuming function, and the interplay of psychological and behavioural factors are important as for any chronic pain condition.

Physical therapists with experience in complex regional pain syndrome routinely use psychological strategies and psycho-education incorporated with the physical intervention.

If the patient fails to make progress (acute phase) or once the condition becomes chronic, a **formal psychological assessment** should be offered.

Specific therapies can be considered and tailored for the patient as part of a holistic approach.

Strategies have included:

- Relaxation techniques

- Adoption of active rather than passive coping strategies

- Cognitive behavioural therapy

    - ♥ Cognitive behavioural therapy (six sessions) in children has been added to outpatient physiotherapy, with positive effects.

- Acceptance and commitment therapy.

These psychological interventions attempt to address any external factors or incentives that can positively or negatively influence the patient's problems. Claims for compensation for example may add a patient's stress.

Psychiatric therapy:

This may be required for patients with chronic symptoms who develop significant depression.

Disposition:

If the diagnosis is suspected then referral pathways in the first instance may include:

- Orthopaedic
- Rheumatology
- Chronic Pain Clinics

References

1. Greta Palmer, Complex Regional Pain Syndrome. Aust Presc 2015; 38:82 - 6.

Dr J. Hayes
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