

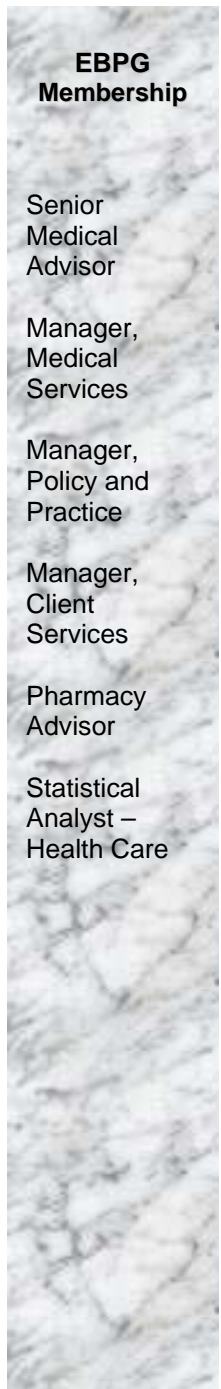


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June 19, 2006

Re: CRPS (Complex Regional Pain Syndrome), First Update.

We have once again reviewed the up-to-date literature on CRPS diagnostic criteria. The August 2005 International Association for the Study of Pain (IASP) conference in Sydney, Australia, discussed this issue. Based on those proceedings and others, we continue to feel that our earlier WorkSafeBC diagnostic criteria for CRPS remain valid and appropriate. Please review these criteria and the background documentation at:

http://www.worksafebc.com/health_care_providers/related_information/evidence_based_medicine/default.asp

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CWM/kt

C R P S.

(Complex Regional Pain Syndrome)

**Towards the development of Diagnostic Criteria and
Treatment Guidelines**

First Update.

By

WCB Evidence Based Practice Group

Dr. Craig W. Martin, Senior Medical Advisor

March 2006



**Clinical Services,
Worker and Employer Services**

Complex Regional Pain Syndromes (CRPS)

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The Evidence Based Practice Group



Objectives.

- Overview on CRPS:
 - History,
 - Epidemiology,
 - Diagnostic criteria,
 - Treatment

Overview.

- CRPS:
 - history, epidemiology, pathophysiology
- Diagnostic criteria:
 - Veldman's 1993, IASP 1994, Bruehl's 1996, AMA 2001, WorkSafeBC 2004, Presley Reed 2005, UK Orthopaedics 2005, IASP 2005
- Treatment:
 - Pharmacological, surgical

CRPS.

- History:
 - 1634, Ambroise Paré described a clinical syndrome that later became known as reflex sympathetic dystrophy
 - Claude Bernard 1st mentioned a syndrom characterized by the association of pain and the sympathetic nervous system
 - 1862, Paget described patients with 'distressing' pains in the fingers after nerve injury that had associated 'nutritional changes'
 - 1867, Silas Weir-Mitchell coined the term 'causalgia' to describe a pain syndrome affecting soldiers who had sustained nerve injuries during the American Civil War

- 1901, Südeck described a syndrome characterized by bone changes after injury
- 1946, Evans applied a generic term 'reflex sympathetic dystrophy' (RSD) in describing a group of patients with chronic pain associated with skin changes
- 1993, Orlando, the International Association for the Study of Pain (IASP), consensus group of experts, renamed RSD as Complex Regional Pain Syndromes (CRPS) type 1 (RSD) and 2 (causalgia)

- CRPS is also known as:
 - RSD, Südeck's atrophy, algodystrophy, shoulder hand syndrome, painful post traumatic osteoporosis, minor causalgia, algoneurodystrophy, post traumatic pain syndrome, painful post traumatic dystrophy, transient migratory osteoporosis → now known as CRPS type 1
 - Causalgia, major causalgia, Mitchell's causalgia → now known as CRPS type 2

- **Definition of CRPS:**

- is a syndrome that describes a broad spectrum of sensory, autonomic, and motor features predominantly present in the extremities
- is a disabling chronic pain condition of unknown etiology
- is a functional disorder of the spinal cord that involves to varying degree the dorsal and ventral horns, as well as the intermediolateral columns, so as to produce sensory, motor, and autonomic abnormalities. The original dysfunction may spread to the adjacent spinal cord level and can cross the midline and travel from cord segments serving lower to upper limbs and vice versa
- the term CRPS is meant to describe certain chronic pain syndromes and does not embody any assumptions about cause or pathophysiology (WorkSafeBC)

- **IASP definition of CRPS:**

- Condition initiated by an injury
- Not limited to distribution of single peripheral nerve
- Pain disproportionate to inciting event
- Associated at some point with
 - edema
 - changes in skin, blood flow
 - abnormal sweating
 - or allodynia
 - or hyperalgesia
- Site usually distal extremity with a DISTAL to PROXIMAL gradient

- The central difference between CRPS type I and type II:
 - Type II occurs following a known peripheral nerve injury with damage to nerve function
 - Type I occurs in the absence of any known nerve injury
 - Signs and symptoms for both are clinically indistinguishable
- Some experts suggested that CRPS is a neuropathic pain

- **Epidemiology:**
 - CRPS is usually precipitated by noxious stimulation or immobilization in the periphery, although the amount of tissue damage may be minimal
 - Incidence of CRPS varies enormously from 0.05% to 35% depending on the population surveyed and/or the diagnostic criteria used.
 - It is estimated that 20% - 35% of these cases will remain incapacitated and only 20% - 30% return to their previous level of function.
 - Mean age varies from 36 – 42 years old
 - Females predominate in a range of 60% - 80%.
 - Precipitating injury maybe major, minor (e.g. sprain) or even unknown
 - Although pain is the cardinal feature of CRPS, some experts presented/suggested cases of CRPS without pain

- **Pathophysiology:**

- Generally accepted as a neurologic disorder affecting both central and peripheral nervous systems
- Exact pathophysiology is still unclear
- Hypothesized mechanisms include:
 - Factors affecting afferent neural system due to sensitization of damaged primary nociceptive afferent fibers and/or sensitization of central nociceptive pathways (esp. in the dorsal horn)
 - Factors affecting the sympathetic system including abnormalities in discharge patterns and or changes in sympathetic target organs
 - Neuronal coupling (sympathetic postganglionic and primary afferents) due to direct chemical coupling and/or coupling in traumatized nerves and/or coupling in dorsal root ganglion large-diameter afferent neurons and/or indirect coupling through vascular beds or non-neural cells

- **Hypothesized mechanisms cont...:**

- Motor system changes due to abnormalities in discharge patterns of α and γ motor neurons
- Genetic predisposition
- Other mechanisms such as exaggerated inflammatory response or protective disuse or myofascial dysfunctions
- It is suggested that:
 - Multiple mechanisms involving various regions of entire neuraxis underlie the development of CRPS
 - Pathophysiology may vary from one patient to another

Overview.

- **CRPS:**
 - history, epidemiology, pathophysiology
- **Diagnostic criteria:**
 - Veldman's 1993, IASP 1994, Bruhl's 1996, AMA 2001, WorkSafeBC 2004, Presley Reed 2005, UK Orthopaedics 2005, IASP 2005
- **Treatment:**
 - Pharmacological, surgical

Diagnostic criteria.

- Has evolved across time – and will likely continue to do so.
- Pain is the hallmark of CRPS.
 - in most cases, pain is preceded by a noxious event
 - pain is out of proportion to the inciting event
 - spontaneous pain occurs in > 90% of CRPS patients
 - pain maybe described as burning, deep, aching, throbbing, sharp, shooting or tearing

- **Veldman's criteria:**

- Based on observations of 829 prospectively recruited patients (the largest case series so far)
- **Criteria:**
 - 4 or 5 of: unexplained diffuse pain, difference in skin color relative to other limb, diffuse edema, difference in skin temperature relative to other limb, limited active ROM
 - occurrence or increase of above signs and symptoms after use
 - above signs and symptoms present in an area larger than the area of primary injury or operation and including the area distal to the primary injury

- **IASP 1994 criteria:**

1. the presence of an initiating noxious event, or a cause of immobilization
2. continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event
3. evidence at sometime of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain
4. this diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction

Type 1: without evidence of major nerve damage

Type 2: with evidence of major nerve damage

Criteria 2 -4 are necessary for the diagnosis of CRPS

- Bruehl's 1996 criteria:

- Clinical signs and symptoms:
 - **Positive sensory abnormalities:** spontaneous pain, mechanical hyperalgesia, thermal hyperalgesia, deep somatic hyperalgesia
 - **Vascular abnormalities:** vasodilation, vasoconstriction, skin temperature asymmetries, skin color changes
 - Edema, sweating abnormalities, swelling, hyperhidrosis, hypohidrosis
 - **Motor/trophic changes:** motor weakness, tremor, dystonia, coordination deficits, nail/hair changes, skin atrophy, joint stiffness, soft tissue changes

- Bruehl's 1996 criteria cont..

- Interpretation:
 - clinical use: ≥ 3 symptoms from each category and ≥ 2 signs from each category
 - sensitivity 0.85, specificity 0.60
 - research use: ≥ 4 symptoms from each category and ≥ 2 signs from each category
 - sensitivity 0.70, specificity 0.96
- The application of sensitivity and specificity in this case is somewhat misleading

- AMA 2001 criteria:
 - Local clinical signs:
 - Vasomotor changes: skin color mottled or cyanotic, skin temperature cool, edema
 - Sudomotor changes: skin dry or overly moist
 - Tropic changes: skin texture smooth, non elastic; soft tissue atrophy esp. in finger tips; joint stiffness and decreased passive motion; nail changes → blemished, curved, talon like; hair growth changes → fall out, longer, finer
 - Radiographic signs:
 - Radiographs: tropic bone changes, osteoporosis
 - Bone scan: findings consistent with CRPS

- AMA 2001 criteria cont..
 - Interpretation:
 - ≥ 8 → probable CRPS
 - < 8 → no CRPS

- **WorkSafe BC 2004 criteria:**

1. The patient must have continuing pain that is disproportionate to any inciting event.
2. The patient must report at least one symptom in at least three out of the following four categories in the affected extremity:
 - Sensory: reports of hyperesthesia
 - Vasomotor: reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry
 - Sudomotor/edema: reports of edema (with or without joint stiffness) 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 (nails, hair, skin)

- **WorkSafe BC 2004 criteria cont..**

3. The patient must display at least one sign in two or more of the following categories in the affected extremity:
 - Sensory: evidence of hyperalgesia (to pinprick) or allodynia (to light touch)
 - Vasomotor: evidence of temperature asymmetry and/or skin color changes and/or asymmetry
 - Sudomotor/edema: objective evidence of edema (with or without joint stiffness) and/or sweating changes and/or sweating asymmetry
 - Motor/trophic: evidence of decreased range of motion (including joint stiffness) and/or motor dysfunction and/or trophic changes

- Presley Reed 2005 criteria:

- **History:**

- report intense, constant, burning pain that is present without stimulation or movement
- pain occurs beyond the territory of single peripheral nerve
- pain disproportionate to the inciting event
- physical signs and symptoms wax and wane (a limb maybe normal temperature one day and cold the next)

- **Physical exam** can exhibit:

- swelling
- local changes of skin color (pale to purple)
- local sweating changes
- local temperature changes
- changes in nail and hair growth

- Presley Reed 2005 criteria cont..

- **Physical exam** can exhibit cont..

- reduce ROM and joint flexibility
- local alteration of skin texture of smooth or shiny in the affected extremity
- these signs come and go, sometimes on a daily basis

- **Tests:**

- triple phase bone scan maybe used to reveal osteoporosis or increased circulation in the joints in the affected areas
- thermography test may reveal differences in skin temperatures between the affected and unaffected body parts
- x-ray may demonstrate loss of bone minerals
- positive laboratory tests are definitive but negative tests do not rule out CRPS

- Presley Reed 2005 criteria cont..
 - Objective criteria for CRPS are comprised of **8 criteria: 6 clinical signs and 2 radiographic signs.**
 - The 6 clinical signs are swelling, local skin color changes (pale to purple), local sweating changes, local temperature changes, reduce ROM and joint flexibility, local alteration of skin texture of smooth or shiny in the affected extremity
 - A stimulus test (with touch, pinprick, heat or cold) to gauge the pain level at the affected site may aid in the diagnosis.

- UK Orthopaedics 2005 criteria:
 - the diagnosis is made clinically by the finding of the following abnormalities which should not be readily explained by the underlying orthopaedic condition:
 - **neuropathic pain:** non dermatomal, without cause, burning, with associated allodynia and hyperpathia
 - **vasomotor instability and abnormalities of sweating:** warm red and dry, cool blue and clammy or an increase in temperature sensitivity. Associated with an abnormal temperature differences between the limbs
 - **swelling**
 - **loss of joint mobility**
 - **joint and soft tissue contracture**
 - these clinical findings are backed up by:
 - radiographic evidence of osteoporosis after 3 months
 - increased uptake on bone scintigraphy early in CRPS

- IASP 2005 publication criteria:

- A. factor 1. hyperalgesia signs, hyperaesthesia symptoms, allodynic signs
 - B. factor 2. temperature asymmetry symptoms, color change signs, color change symptoms
 - C. factor 3. edema signs, sweating asymmetry signs, edema symptoms
 - D. factor 4. decreased range of motion signs, decreased range of motion symptoms, motor dysfunction signs, motor dysfunction symptoms, trophic symptoms, trophic signs
- This is based on factor analysis on a series of 123 patients
 - Still not formally adopted by IASP

- The 2005 IASP refresher course is in fact still employing the 1996 Bruhl's criteria

- the course stated that there is no diagnostic gold standard nor an objective test for CRPS
- the course emphasized the importance of patient history and physical examination as the basis of CRPS diagnosis
- the course mentioned the high *sensitivity* of temperature differences, as well as the high *specificity* of plain radiograph, bone scan, quantitative sensory imaging and MRI.

- It should be noted that:
 - to date there is no gold standard in diagnosing CRPS
 - studies show the inconsistent application of CRPS diagnostic criteria
 - studies show poor agreement between clinicians in diagnosing CRPS (in the same sample)
 - the application of sensitivity and specificity in evaluating different set of diagnostic criteria may be misleading

Overview.

- **CRPS:**
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- **Treatment:**
 - Pharmacological, surgical

Treatment.

- Lack of understanding of the underlying pathophysiology and lack of objective diagnostic criteria hamper clinical trials of therapeutic modalities.
- 2002 comprehensive systematic review (level 1 evidence) on the treatment of CRPS type 1 found:
 - 27 RCTs were included
 - studies were heterogenous in various aspects
 - small sample sizes
 - cautious conclusion of limited to no evidence on the efficacy of stellate ganglion or regional block, radical scavenging (topical dimethylsulfoxide) prednisolone, acupuncture and manual lymph drainage.
 - Calcium-regulating drugs and tai chi maybe effective

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- 1998 expert consensus stated that treatment should be developed around functional restoration
- most patients will improve as long as sufficient analgesia and symptomatic control can be provided to support the exercise therapy
- 2002 update → 3 basic treatment measures are required:
 - pain management
 - rehabilitation
 - psychological therapy
- One study identified relative pain reduction of 50% and an absolute pain reduction of at least 3 (out of 10) on the VAS as clinically meaningful among CRPS patients
- Osenbach remarked that ..indeed most studies of CRPS are small anecdotal clinical studies that present little scientific data..

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Pharmacological therapy.

- NSAIDs (level 4 evidence):
 - have not been investigated in CRPS patients
- Opioids (level 4 evidence):
 - have not been studied
- Antidepressants (level 4 evidence):
 - either TCA or SSRI have never been studied in CRPS patients
- Sodium channel blockers (level 4 evidence):
 - IV lidocaine effective in reducing spontaneous and evoked pain

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- GABA agonists (level 4 evidence):
 - intrathecal baclofen effective in treating dystonia
 - no evidence on the analgesic effect of oral baclofen, valproic acid, vigabatrin, benzodiazepines
 - gabapentine effective in reducing pain
- Steroids (level 4 evidence):
 - oral prednisone 10 mg tid effective in improving clinical status
- NMDA-receptor blockers (level 4 evidence):
 - e.g. ketamine, DMP, amantadine, memantine have not been studied in CRPS
- Calcium regulating drugs (level 4 evidence):
 - intranasal calcitonin reduced pain significantly

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- Free radical scavengers (level 4 evidence):
 - dimethylsulfoxide (DMSO) or N-acetylcysteine effective in reducing pain

Interventional therapy.

- Sympathetic ganglion blocks (level 4 evidence):
 - not effective
- IV regional block (level 4 evidence):
 - reserpine, guanethidine, lidocaine, prilocaine, droperidol not effective
 - bretylium+lidocaine may be effective
 - bolus ketanserin may be effective
- Bier block (level 1 evidence):
 - with methylprednisolone + lidocaine not more effective than saline

- **Surgical sympathectomy (level 4 evidence):**
 - limited evidence on its efficacy (best predictor if procedure done within 12 months of inciting factors)
- **TENS (level 4 evidence):**
 - may be effective
- **SCS (level 4 evidence):**
 - may be effective
 - (may be effective in pain but not in function. See the EBPB's own review on this topic)
- **Motor cortex stimulation (level 4 evidence):**
 - may be effective in reducing pain, weakness and increasing mobility

Other treatment modalities.

- **Physical therapy (level 4 evidence):**
 - standardized physiotherapy can provide long term relief of pain and improvement of physical dysfunction in children
 - physiotherapy may reduce pain and improve active mobility in adults
- **Occupational therapy (level 4 evidence):**
 - OT may reduce pain and improve active mobility in adults in lesser extent than PT
- **Psychological therapy (level 4 evidence)**
 - CBT + PT may provide long lasting reduction of all symptoms

- Acupuncture (level 4 evidence):
 - conflicting evidence
- Tai Chi (level 4 evidence):
 - may be effective

Cochrane Reviews (level 1 evidence).

- Local anesthetic sympathetic blockade:
 - not enough data, its usefulness is questionable
- SCS:
 - SCS may be effective in certain patients. However, there is little evidence to assess the benefits and harms of this treatment
- Sympathectomy:
 - evidence for its effectiveness is very weak and based on poor studies

- **Systemic local anesthetic agents:**
 - lidocaine and mexiletine were superior than placebo in treating diabetic neuropathy, post herpetic neuralgia and cancer related neuropathic pain (not for CRPS in particular)
 - see our review on this in the WSN

QUESTIONS ?

SUGGESTIONS ?

THANK YOU !

Bibliography

1. Forouzanfar T, Koke AJA, van Kleef M, Weber WEJ. Treatment of complex regional pain syndrome type I. *European Journal of Pain*. 2002; 6:105-122.
2. Birklein F, Handwerker HO. Complex regional pain syndrome: how to resolve the complexity? *Pain*. 2001;94:1-6.
3. Harden RN, Bruehl S, Galer BS, Saltz S, Bertram M, Backonja M, Gayles R, Rudin N, Bhugra MK, Stanton-Hicks, M. Complex regional pain syndrome: are the IASP diagnostic criteria valid and sufficiently comprehensive? *Pain*. 1999;83:211-219.
4. Galer BS, Bruehl S, Harden RN. IASP Diagnostic Criteria for Complex Regional Pain Syndrome: A Preliminary Empirical Validation Study. *The Clinical Journal of Pain*. 1998;14:48-54.
5. Eisenberg E, Melamed E. Can complex regional pain syndrome be painless? *Pain*. 2003;106:263-267.
6. Hayek SM, Mekhail NA. Complex Regional Pain Syndrome. *The Physician and Sportsmedicine*. May 2004;32(5 -..)
7. Teasdall RD, Smith BP, Koman LA. Complex regional pain syndrome (reflex sympathetic dystrophy). *Clinical Sports Medicine*. 2004;23:145-155.
8. Zyluk A. Complex Regional Pain Syndrome Type I. Risk Factors, Prevention and Risk of Recurrence. *Journal of Hand Surgery (British and European Volume)*. 2004;29B:4:334-337.
9. Hartrick CT. Mechanism-based Treatment for Complex Regional Pain Syndrome: Back to Basics. *Pain Practice*. 2004;4(2):69-73.
10. Burton AW, Hassenbusch, SJ, Warneke, C, Racz, G, Stanton-Hicks, M. Complex Regional Pain Syndrome (CRPS): Survey of Current Practices. *Pain Practice*. 2004;4(2):74-83.
11. Osenbach RK. Complex Regional Pain Syndromes. *Seminars in Neurosurgery*. 2004;18(1):81-92.
12. Wasner G, Schattschneider J, Binder A and Baron R. Complex regional pain syndrome – diagnostic, mechanisms, CNS involvement and therapy. *Spinal Cord*. 2003;41:61-75.
13. Backonja M-M, Serra J. Pharmacologic Management Part 2: Lesser-Studied Neuropathic Pain Diseases. *Pain Medicine*. 2004;5(S1):S48-S59.
14. Stanton-Hicks M. Complex regional pain syndrome. *Anesthesiology Clinics of North America*. 2003;21:733-744.
15. Harden RN. Pharmacotherapy of Complex Regional Pain Syndrome. *American Journal of Physical Medicine and Rehabilitation*. 2005;84:S17-S28.
16. Bruehl S, Harden RN, Galer BS, Saltz S, Backonja M, Stanton-Hicks M. Complex regional pain syndrome: are there distinct subtypes and sequential stages of the syndrome? *Pain*. 2002;95:119-124.
17. Perez RSGM, Keijzer C, Bezemer PD, Zuurmond WWA, de Lange JJ. Predictive value of symptom level measurements for complex regional pain syndrome type I. *European Journal of Pain*. 2005;9:49-56.

18. Janig W, Baron R. Is CRPS I a neuropathic pain syndrome? Editorial. *Pain*. 2006;120:227-229.
19. Harney D, Magner JJ, O'Keefe D. Complex regional pain syndrome: the case for spinal cord stimulation (a brief review). *Injury, International Journal of the Care of the Injured*. 2005;36:357-362.
20. McBride A, Atkins R. Complex regional pain syndrome. *Current Orthopaedics*. 2005;19:155-165.
21. Veldman PHJM, Reynen HM, Arntz I, Goris RJA. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. *The Lancet*. Oct 1993;342:1012-1016.
22. Forouzanfar T, Weber WEJ, Kemler M, and van Kleef M. What Is a Meaningful Pain Reduction in Patients With Complex Regional Pain Syndrome Type 1? *The Clinical Journal of Pain*. 2003;19:281-285.
23. Baron R, Janig W. Complex regional pain syndromes – how do we escape the diagnostic trap? *The Lancet*. Nov 13, 2004;364:1739-1741.
24. Pearce JMS. Chronic regional pain and chronic pain syndromes. *Scientific Review. Spinal Cord*. 2005;43:263-268.
25. van de Vusse AC, Stomp-van den Berg SGM, de Vet HCW, Weber WEJ. Interobserver reliability of diagnosis in patients with complex regional pain syndrome. *European Journal of Pain*. 2003;7:259-265.
26. van de Beek WJT, Schwartzman RJ, van Nes SI, Delhaas EM and van Hilten JJ. Diagnostic criteria used in studies of reflex sympathetic dystrophy. *Neurology*. 2002;58:522-526.
27. Taskaynatan MA, Ozgul A, Tan AK, Dincer K and Kalyon TA. Bier Block With Methylprednisolone and Lidocaine in CRPS Type I: A Randomized, Double-Blinded, Placebo-Controlled Study. *Regional Anesthesia and Pain Medicine*. Sep-Oct 2004;29(5):408-412.
28. Quisel A, Gill JM, Witherell P. Complex regional pain syndrome underdiagnosed. *The Journal of Family Practice*. Jun 2005;54(6):524-532.
29. Atkins RM. Aspects of current management. *Complex Regional Pain Syndrome. The Journal of Bone and Joint Surgery (Br)*. 2003;85-B:1100-1106.
30. Baron R, Binder A, Ludwig J, Schattschneider J and Wasner GL. Diagnostic Tools and Evidence-Based Treatment of Complex Regional Pain Syndrome. In: Justins DM (ed.). *Pain 2005. An updated review. Refresher Course Syllabus. 11th World Congress on Pain. IASP Press. Seattle*. pp. 293-306.
31. Complex Regional Pain Syndromes. In: Charlton, JE (ed). 2005. *Core Curriculum for Professional Education in Pain. IASP Press, Seattle*, pp..
32. .. Complex Regional Pain Syndrome. In: Reed P (Editor-in-Chief). (2005). *The Medical Disability Advisor. Workplace Guidelines for Disability Duration. 5th ed. Vol 1. Reed Group Ltd. Westminster, Colorado*. pp.541-543..
33. Cocchiarella L, Andersson GBJ (eds) (2000). *Guides to the Evaluation of Permanent Impairment. 5th ed. AMA Press. USA*.
34. Wilson PR, Stanton-Hicks M, Harden RN. (eds) (2005). *CRPS: Current Diagnosis and Therapy. Progress in Pain Research and management. Vol 32. IASP Press. Seattle*.

35. Loeser JD (ed). (2001). *Bonica's Management of Pain*. 3rd ed. Lippincott Williams & Wilkins. Philadelphia.
36. Harden RN, Bruehl S. Diagnostic Criteria: The Statistical Derivation of the Four Criterion Factors. In: Wilson P, Stanton-Hicks M, and Harden RN (eds) (2005). *CRPS: Current Diagnosis and Therapy, Progress in Pain Research and Management*. IASP Press. Seattle. pp. 45-58.
37. Challapalli V, Tremont-Lukats IW, McNicol ED, Lau J, Carr DB. Systemic administration of local anesthetic agents to relieve neuropathic pain. *The Cochrane Database of Systematic Reviews* 2005, Issue 4, Art. No.: CD003345.pub2.
38. Wiffen PJ, McQuay HJ, Edwards JE, Moore RA. Gabapentin for acute and chronic pain. *The Cochrane Database of Systematic Reviews* 2005, Issue 3, Art. No.: CD005452.
39. Mailis-Gagnon A, Furlan A. Sympathectomy for neuropathic pain. *The Cochrane Database of Systematic Reviews* 2002, Issue 1. Art. No.: CD002918.
40. Mailis-Gagnon A, Furlan AD, Sandoval JA, Taylor R. Spinal cord stimulation for chronic pain. *The Cochrane Database of Systematic Reviews* 2004, Issue 3, Art. No.: CD003783.pub2.
41. Cepeda MS, Carr DB, Lau J. Local anesthetic sympathetic blockade for complex regional pain syndrome. *The Cochrane Database of Systematic Reviews* 2005, Issue 4, Art. No.: CD004598.pub2.