



**Mirror, Mirror on the Wall:
Graded Motor Imagery to Treat CRPS**

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Disclosures

- None



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Learning Objectives

- Describe the Budapest criteria for the diagnosis of CRPS.
- Review the treatment options available for CRPS.
- List the components of Graded Motor Imagery in proper order.

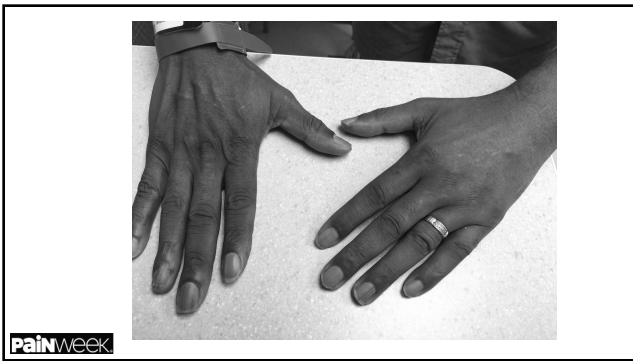


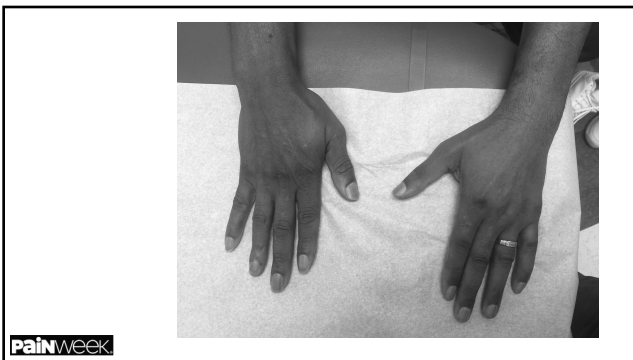
Outline

- History
- Epidemiology
- Clinical Presentation
- Proposed Pathophysiology
- Diagnosis and Differential
- Treatment









Causalgia



Silas Weir Mitchell
1829 - 1914



Philadelphia,
Lippincott, 1864

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Causalgia

The term causalgia was coined at that time after the Greek words *kausis*, meaning burning, and *algos*, meaning pain.

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Causalgia - Weir Mitchell

"Long after the trace of the effects of a wound has gone . . . neuralgic symptoms are apt to linger, and too many carry with them throughout long years this final reminder of the battle-field."



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Nerve Injuries: Lesions of Sensation

- Case 24: H.W. 42, shot in left arm, injured ulnar nerve
 - “50 days later-- Pain below elbow down into the hand, burning and tingling. . . It is intense and increasing.
 - Entire hand sore to touch . . . but tact is unimpaired.
 - The hand is swollen. . . the palm is red.
 - The patient has kept the hand wet ever since he was hurt.”

- Hyperaesthetic conditions
- Anesthetic conditions
- Neuralgia - Burning



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Sudeck

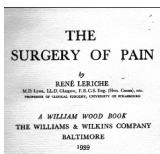


Paul Sudeck
1866-1945

- In 1900, Sudeck noted muscle atrophy and demineralization of bone:
 - Described as, “patchy osteoporosis of the small bones of the hands or feet and the distal metaphysis of the forearm or tibial bones.”
 - This gave rise to the term *Sudeck's dystrophy*.

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Leriche



- A lady, aged 37, receive a gift of a hare. She cut it up, with a view to make a well-known marinade. . . she pricked her index finger with a spicule of bone.
- “By next day, all trace of injury had vanished and it was forgotten. The hare was eaten, but it had its revenge!”

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Leriche R. 1939; p 119

Complex Regional Pain Syndrome

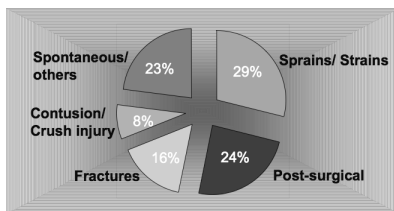
- Does not consistently show sympathetic involvement, reflex mechanism, or dystrophy.
- Special Consensus Group of the International Association for the Study of Pain (IASP) termed *complex regional pain syndrome* in 1994:
 - Allows for a more broad inclusion showing varying levels of the disease process.



Epidemiology



CRPS - Inciting Event Restrospective Review - UW Pain Center



Allen et al. Pain 1999;80:538

Epidemiology

- CRPS can occur at any age,
 - Pediatric patients constituting < 10%

- Common in younger adults
 - Mean 41.8 years
 - Mean age at time of injury 37.7 years



Allen et al. Pain 1999;80:538

Epidemiology

- The incidence of CRPS (CRPS 1 and 2) estimated to be 6.28/100,000
- 2.3 - 3 times more frequent in females than males
- Usually involves a single limb in the early stage
- Mean duration of symptoms before pain center evaluation = 30 months



Estimated CRPS Cases per Year after Orthopedic Surgery

Procedure	Number/yr	Rate	CRPS /yr
Arthroscopic Knee surgery	657,000	2.3-4%	15-26,000
Carpal Tunnel	366,000	2.1-5%	8-18,000
Ankle fracture	257,000	13.6%	35,000
Total knee replace.	247,000	0.8-13%	2-32,000
Wrist fractures	194,000	7-37%	14-72,000
Fasciectomy-Dupuytren's contra.	20,000	4.5-40%	1-8,000
TOTAL	1,741,000	4.3-11%	74-191,000



Gottschalk A, Raja SN Anesthesiology 2004

Severity Correlation

- There is no distinct correlation between the severity of trauma and the degree of CRPS symptoms.

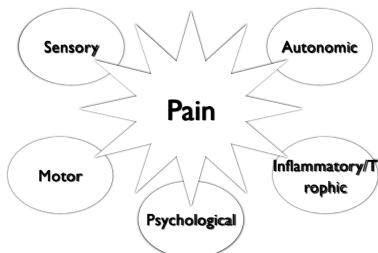


Stanton-Hicks M, Janig W, et al. Pain 1995

Clinical Presentation



Clinical Aspects of CRPS

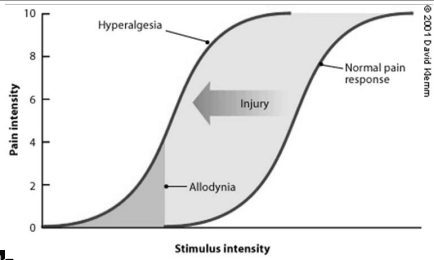


Sensory Changes in CRPS

- Allodynia
- Hyperalgesia



Pain Sensitization



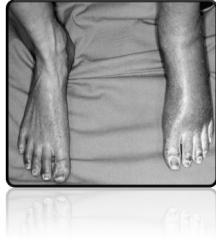
Sensory Changes in CRPS

- Allodynia
- Hyperalgesia
- Hyperesthesia
 - Increased sensitivity to a sensory stimulation
- Hyperpathia
 - Abnormally exaggerated subjective response to painful stimuli



Autonomic Signs in CRPS

- Edema (80% of all cases)
- Color change
- Temperature (warmer or cooler – 80%)
- Sweating (↑ or ↓)



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Motor Symptoms and Signs in CRPS



Tremor, Weakness, Contractures

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Trophic Changes

- Altered nail growth
- Altered hair growth
- Skin changes



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Signs & Symptoms in Early and Late CRPS

Inflammatory S & S	2-6 months	>12 months
Pain	88 %	97 %
Color difference	96 %	84 %
Edema	80 %	55 %
Temperature diff.	91 %	91 %
Limited movement	90 %	83 %
↑ pain with exercise	95 %	97 %

Total= 829 pts. Veldman et al. Lancet 1993;342:1012



Severe Complications of CRPS

7.4%	N (total)	Upper extremity	Lower extremity
Infection	30	30%	70%
Ulcers	26	11%	89%
Chronic edema	27	11%	89%
Dystonia	50	38%	62%
Myoclonus	21	43%	57%
All complications	154	28%	72%

Total of 74 patients

van der Laan et al, 1998



Psychological Changes

- Fear
- Anxiety
- Anger
- Suffering
- Depression
- Failure to Cope



Raja SN et al. Anesthesiology 2002



CRPS and the Psyche Facts and Fallacies

- CRPS is a psychiatric illness
- CRPS causes a psychiatric illness
- Psychiatric illness or personality disorder are predisposing factors for CRPS
- Psychological factors modify the course of CRPS
- Adjustment and function in CRPS are worsened by maladaptive behavior



Covington EC 2002

CRPS Can Spread

- Contiguous Spread
 - Gradual, significant enlargement of the affected area
- Independent Spread
 - CRPS appears in a distant, non-contiguous area
- Mirror-Image Spread
 - Symptoms appear on the opposite side in an area that closely matches size and location of original side



Maleki J et al. 2000

Is CRPS a Systemic Disease?



A patient with both upper and lower extremity CRPS being affected at different times about two years apart.



Pathophysiology

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Pathophysiology

- Inflammation
- Autonomic Dysfunction
- Neuroplastic Changes in the CNS
- Ischemia/Reperfusion Injury

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Pathophysiology

- Inflammation
 - Neurogenic
 - Substance P – plasma protein extravasation
 - CGRP – vasodilation
 - Inflammatory Cytokines (TNF- α , IL-2)

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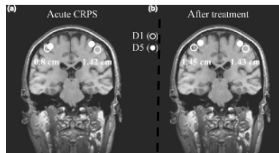
Pathophysiology

- Autonomic Dysfunction
 - Acute stage – sympathetic vasoconstrictor reflexes are inhibited
 - Chronic Stage – vasoconstriction and cold skin
 - Leads to impaired capillary nourishment



Pathophysiology

- Neuroplastic Changes



- Ischemia/Reperfusion Injury → 2010 After 1 year of treatment



Maihofner C, et al. Neurology, 2004

Central Nervous System Changes

- Chronic Pain is associated with generalized and regional reduction in gray matter
 - Not found in patients with acute pain
- Percent of atrophy is correlated with the duration of pain

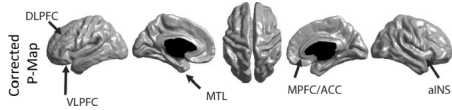


Central Nervous System Changes

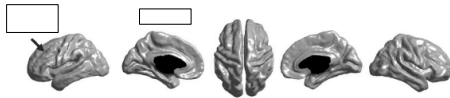
- Consistently altered in chronic pain: (Apkarian, 2004)
 - Cingulate cortex
 - Motivation & emotional response to pain
 - Insula
 - Estimation of the magnitude of pain
 - Awareness of body states
 - Dorsolateral prefrontal cortex
 - Integration of sensory input
 - Short-term working memory



Cortical thinning in CLBP compared to controls

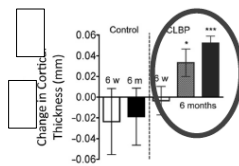


Reversal of cortical thinning with treatment of pain



Seminowicz, 2011

Reversal of cortical thinning with treatment of pain

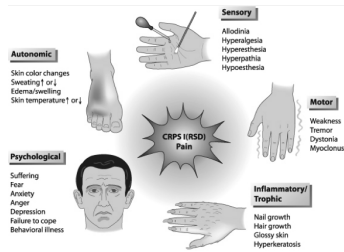


Seminowicz, 2011

Diagnosis and Differential



Clinical Features of CRPS



IASP Diagnostic Criteria

- Presence of an initiating noxious event or reason for immobilization.
- Disproportional pain, allodynia, or hyperalgesia from a known inciting event.
- Signs or symptoms of any evidence showing edema, skin changes, blood flow, or abnormal sudomotor activity in the region of the pain.
- No other condition that would otherwise explain the degree of pain or dysfunction



IASP Diagnostic Criteria

- Developed in 1994
- Too vague
- How many symptoms?
- How many signs?
- Sensitivity for this diagnostic criteria was high: 0.98
- Unfortunately met with a low specificity: 0.36
- Lead to an over diagnosis of the pain syndrome



Budapest Consensus Criteria 2007

Must report at least 1 symptom in 3 out of 4 categories

<u>Sensory</u> hyperesthesia and/or allodynia	<u>Vasomotor</u> Temperature asymmetry Skin color changes Skin color asymmetry
<u>Motor</u> Decreased ROM, tremor; Weakness, dystonia, trophic changes (hair, nail, skin)	<u>Sudomotor</u> Edema Sweating changes Sweating asymmetry



Budapest Consensus Criteria 2007

Must display at least 1 sign in 2 or more categories

<u>Sensory</u> hyperalgesia and/or allodynia	<u>Vasomotor</u> Temperature asymmetry Skin color changes Skin color asymmetry
<u>Motor</u> Decreased range of motion Weakness, tremor, dystonia Trophic changes (hair, nail, skin)	<u>Sudomotor</u> Edema Sweating changes Sweating asymmetry



Criteria Comparison

▪ IASP criteria showed high diagnostic sensitivity (0.98), but poor specificity (0.36).

▪ In comparison, the Budapest clinical criteria retained the exceptional sensitivity of the IASP criteria (0.99), but greatly improved upon the specificity (0.68).



Harden N et al. 2010

Treatment



Treatment Options

- Anticonvulsants
- Antidepressants
- Alendronate
- Free Radical Scavengers
 - 50% dimethyl sulfoxide (DMSO) cream
 - Vitamin C
- Low Dose Naltrexone



Prevention of CRPS Vitamin C (antioxidant) and Wrist Fractures

- 127 wrist fractures - 500 mg Vit C or placebo for 50 days
- 1 year followup - 4/54 (7%) in Vit C vs 14/65 (22%) in placebo developed CRPS

	Odds ratio	P-value
Fracture type	0.09	0.0037
Complaints in plaster cast	0.1	0.0002
Vit C therapy	4.22	0.04



Zollinger et al. Lancet 1999; 354: 2025

doi:10.1016/j.pain.2015.04.014

Effect of Perioperative Vitamin C Supplementation on Postoperative Pain and the Incidence of Chronic Regional Pain Syndrome: A Systematic Review and Meta-analysis.

Chen S¹, Roffey DM, Diaz CA, Anil A, Wu EK

@ Author information

Abstract

OBJECTIVES: Postoperative pain can contribute to increased risk for complications and lengthened hospital stays. The objective was to analyze the effects of perioperative vitamin C supplementation on postoperative pain and the development of complex regional pain syndrome I (CRPS I) in patients undergoing surgical procedures.

METHODS: A systematic review of published literature was performed through April 2014. References from relevant studies were scanned for additional studies. Results were screened for relevance independently, and full-text studies were assessed for eligibility. Reporting quality was assessed using a modified Newcastle-Ottawa Scale.

RESULTS: The search strategy yielded 710 studies, of which 13 were included: seven on postoperative pain and six on CRPS I. In the final analysis, one relevant study found a reduction in postoperative morphine utilization after preoperative vitamin C consumption, while another showed no difference in postoperative pain outcomes between the vitamin C and control groups. A meta-analysis of three applicable CRPS I studies showed a decrease in postoperative CRPS I after perioperative vitamin C supplementation (relative risk (RR)=2.25, tau=0).

DISCUSSION: There is moderate level evidence supporting the use of a 2 g preoperative dose of vitamin C as an adjunct for reducing postoperative morphine consumption, and high level evidence supporting perioperative vitamin C supplementation (2 g per day for 50 days) for CRPS I prevention after extremity surgery. Additional studies are necessary to increase the level of evidence to determine the overall effectiveness and optimum dosage of vitamin C.



doi:10.1016/j.pain.2015.04.014

DOI 10.1007/s10071-014-2517-2

REVIEW ARTICLE

The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain

Jarred Younger · Luke Parkinoy · David McLain

- The typical dosage of LDN in published research is 4.5 mg.
- Hypothesis: naltrexone operates via glial cells to exert beneficial actions. Dextro-naltrexone is a stereoisomer of naltrexone which is active at microglia receptors but has no activity on opioid receptors.



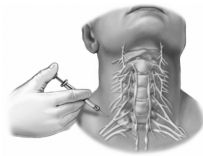
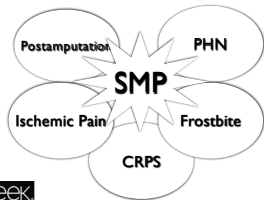
Treatment Options

- Baclofen
- Calcitonin – conflicting data
- Vasodilatory drugs – No evidence
 - Ex. Verapamil, ketanserin



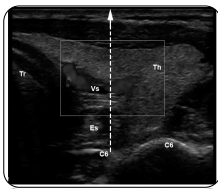
Do Nerve Blocks Help in the Diagnosis of CRPS?

- Sympathetic nerve blocks help identify the subset of patients with sympathetically mediated pain.



Stellate Ganglion Block

- Esophagus lateral to airway in 50% and 74% of the subjects at C6 and C7
- Esophagus covered more than half the distance between the airway and the carotid artery in 14% and 44% of the subjects at the C6 and C7 levels.
- Via anterior approach, a major vessel was observed in up to 29% and 43% of patients at the C6 and C7 levels.



Pain Practice 2008; 8(4): 226-240
 Pain Med. 2012;13(1):1181-8
 Can J Anaesth. 2012 Nov;59(11):1040-7.
 Pain Physician 2007 Nov;10(6):747-52

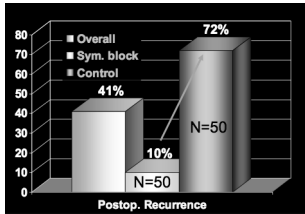


Stellate Ganglion Block



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If I have CRPS, can I undergo surgery without the recurrence of disease?



Retrospective Analysis
 4-16 months after CRPS
 2 separate surgeons
 SGB post-surgery
 One year follow-up

PainWeek

Reuben et al. J Hand Surg 2000;25:1147

Treatment Options

- Sympathectomy
 - Concerns for post-sympathectomy pain syndrome
- Spinal Cord Stimulation
 - Significant reduction in pain at 6, 12, and 24 months after implantation

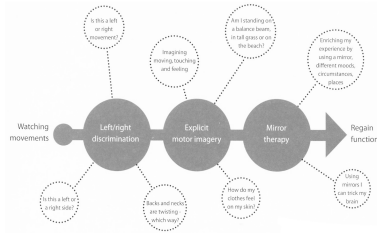
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Kemmler N, et al. Ann Neurol 2004

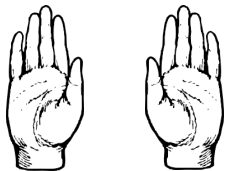
Physical Therapy



Graded Motor Imagery



Limb Laterality

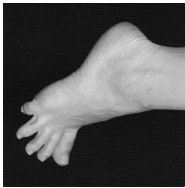


Right or Left?




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Right or Left?



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Explicit Motor Imagery



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Mirror Therapy



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Graded Motor Imagery

- Sequential activation of cortical pre-motor and motor networks
- Laterality and Imagery = pre motor
- Mirror Therapy = Primary Motor Cortex and S1 cortices
- Reversal of cortical reorganization

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Results

- Opioid use: following the treatment process, overall there is a significant reduction in opioid use, $p < 0.001$.
 - Pre GMI: 48 of 92
 - Post GMI 19 of 92
- Functional improvement: following GMI, there is a significant improvement in functionality
 - Median improvement of 32% on quick DASH, $p < 0.001$
 - Median improvement of 22.5% on LEFS, $p < 0.001$
- NRS Scores: Median scores showed significant improvement, $p < 0.001$
 - Pre GMI: 6/10
 - Post GMI: 3.2/10

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Conclusions

- CRPS remains an enigmatic condition.
- Not all patients have the same set of symptoms.
- As it persists, the focus moves toward rehabilitation.
- Treatment with GMI significantly impacts degree of functional recovery and pain improvement in CRPS.