

Complex Regional Pain Syndrome: An Evidence-Based Approach

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OUTCOMES

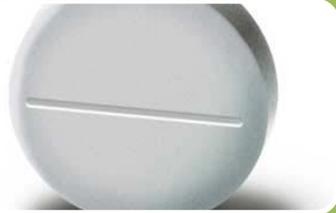
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Today's Presentation Objectives

Our conversation centers on three primary goals.



Understand current, objective diagnostic criteria for complex regional pain syndrome (CRPS)



Understand the treatment strategy for CRPS



Present case management strategies for injured workers given a diagnosis of CRPS

CRPS: Controversies around the diagnosis and treatment

CRPS remains controversial because there are no definitive gold standards for diagnosis and treatment and much remains unknown about what causes it or how to treat it.

- Vague diagnostic criteria historically with overlap of multiple conditions.
- Lack of evidence-based studies on treatment effectiveness:
 - Medications
 - Injections and blocks
 - Spinal cord stimulators and surgical procedures
 - Rehabilitation approaches
- Outcome expectations
- Outcome measurement
- Ability to spread



Overview

- A disease of physical and/or psychological stress affecting the sympathetic nervous system
- Usually limited to one extremity
- Involves pathways of the sympathetic nervous system between the affected limb and the spinal cord with inflammation and irritation of sympathetic nerve branches
- May be accompanied by muscle spasms in the cervical or lumbar regions, pain in the neck and low back, jaw pain, headaches, dizziness, tinnitus, muscle weakness.
- Accompanied usually with skin temperature changes and swelling
- Can lead to osteoporosis if prolonged

CRPS: Definition

Chronic pain that follows a soft tissue or bone injury (type I) or nerve injury (type II) and lasts longer and is more severe than expected from the original tissue damage.

Signs and Symptoms

- Autonomic Changes: Sweating, Vasomotor abnormalities
- Motor Changes: Weakness, dystonia, tremors
- Trophic changes: Skin and bone atrophy, hair loss, thickened hair, joint contractures
- Sensory abnormalities: Hypersensitivity, Allodynia, Hyperalgesia

Epidemiology

May be skewed by incidence of misdiagnosis.

- Incidence 5.5/100,000 in U.S. (compare MS 4/100,000, RA 30/100,000)¹
 - Three times more common in women than men¹
 - 1-2% of fractures
 - 2-5% of people with a peripheral nerve injury develop CRPS
 - 13-70% of those with hemiplegia eventually develop CRPS²
- Risk factors
 - Immobilization¹
 - Stressful social events in 80% of UE CRPS³
 - Smoking increases onset and severity⁴
- Resolution rate, stats vary: 74% by one year vs. 36% resolve within 6 years¹
 - Netherlands, after 6 years only 31% completely incapable of work

1. Clinical features and pathophysiology of complex regional pain syndrome; www.thelancet.com/neurology Vol 10 July 2011 2. Reassessment of the incidence of complex regional pain syndrome type 1 following stroke, *Neurorehabil Neural Repair.* 2000;14(1):59-63 4. Complex Regional Pain Syndrome I (Reflex Sympathetic Dystrophy) Srinivasa N. Raja, M.D.,* Theodore S. Grabow, M.D.† *Clinical Concepts and Commentary Anesthesiology*, V 96, No 5, May 2002. 3. Reflex sympathetic dystrophy and cigarette smoking, *J Hand Surg Am.* 1988 May;13(3):458-60

CRPS: Historical Origins

A pain syndrome linked to sympathetic nerve dysfunction

- Shoulder/Hand syndrome and Causalgia identified during the Civil War
- Sudek's Atrophy (1900)
- Reflex Sympathetic Dystrophy (1947)
- Complex Regional Pain Syndrome: (1994)
 - Scientifically validated diagnostic criteria designed to be inclusive, sensitive, & broad
 - Exclusion of other causes for symptoms¹
 - Focus primarily on symptoms, not so much on signs¹
 - Led to over-diagnosis, still a problem today
 - Criteria found to be very sensitive, but not very specific
 - Resulted in a large number of false positives (specificity range of 36% to 55%)¹

1. Bruehl S, Harden RN, Galer BS, Saltz S, Bertram M, Backonja M, Gayles R, Rudin N, Bhugra MK, Stanton-Hicks M. External validation of IASP diagnostic criteria for Complex Regional Pain Syndrome and proposed research diagnostic criteria. International Association for the Study of Pain. *Pain*. 1999 May;81(1-2):147-54.

The Budapest Criteria

To make a clinical diagnosis, the following criteria must be met.

1. Continuing pain, which is disproportionate to any inciting event
2. Must report at least one symptom in three of the four following categories:
 - Sensory: Reports of hyperesthesia and/or allodynia
 - Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
 - Sudomotor/Edema: Reports of edema 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)

The Budapest Criteria

The new diagnostic criteria increase sensitivity to 0.7 and specificity to 0.94

3. Must display at least one sign at time of evaluation in two or more of the following categories:

- Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
- Vasomotor: Evidence of temperature asymmetry (>1 °C) and/or skin color changes and/or asymmetry
- Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
- Motor/Trophic: Evidence of decreased ROM and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

4. There is no other diagnosis that better explains the signs and symptoms

From the Archives: Is This a Case of CRPS?

Let's investigate the findings and diagnosis.

- 34-year-old man who had a lifting injury and left shoulder dislocation in 2003; shoulder subsequently surgically stabilized and reinjured
- Multiple shoulder arthroscopies; ultimately a shoulder fusion in 2007, later hardware removal
- CRPS diagnosis made for residual pain
- 10 surgeries total, including thoracic outlet syndrome surgery
- Failed spinal cord stimulator, high-dose opioids, topical four-agent compounded cream, ketamine infusions
- Anesthesia pain MD says he is improving and weaning slowly off opioids, yet he is not
- Objective findings consistent with brachial plexus injury



Avoiding Misdiagnosis

Why would doctors misdiagnose CRPS?

- The nature of “syndromes”
- Overreliance on the subjective versus objective
- Misunderstanding of the physiology of CRPS
- Many other conditions can mimic some of the findings of CRPS
- Need a name for unexplained symptoms
- Biomedical practice bias
- Poor interpretation of biological versus psychosocial signs



Summing it Up

Correct diagnosis is the first step to effective treatment.

- CRPS is a real condition, but uncommon
- CRPS has very specific objective criteria
- There are other factors in play causing misdiagnosis of CRPS

Keys to Success in the Early Stages of Case Management



- 1 Know the criteria of true CRPS
- 2 Understand the potential drivers for misdiagnosis
- 3 Intervene by calling for an objective assessment A.S.A.P.
- 4 Find providers expert at objectively assessing and managing CRPS
- 5 Beware of CRPS “experts” with a biomedical bias

Pathophysiology

- Occurs most commonly after a surgical procedure, minor injury, nerve damage, application of ice or prolonged immobilization of a limb such as occurs after casting.



Pathophysiology

- Peripheral pain receptors and CNS sensitization lead to increases central sympathetic activity with release of neuropeptides that then maintain pain and inflammation
- Increased central sympathetic activity and peripheral nociceptor responses to Neurepinephrine lead to heightened SNS tone.

CRPS: Tissue damage and sympathetic activation

- Distinct combination of abnormalities
- Includes limb-confined inflammation and tissue hypoxia, sympathetic dysregulation, small fiber damage, central sensitization and cortical reorganization
- Four cardinal features/findings:
 - pain out of proportion to injury
 - swelling
 - movement abnormalities (including joint stiffness)
 - Color, temperature, and sudomotor changes known as vasomotor instability



Symptoms



Characteristics of the Syndrome

- Highly painful
- Limb-confined condition
- Sensory and motor symptoms, autonomic disturbances, trophic changes
- Variable progression over time
- Usually occurs after trauma
- Associated with a particularly poor quality of life
- Large healthcare and societal costs



Goebel A. Complex Regional Pain Syndrome in Adults. *Rheumatology* 2011;50:1739-1750

What's Complex About CRPS?

- Poorly understood condition by injured workers and many physicians
- Usually triggered as a secondary event to an injury or surgery
- Leaves injured workers frustrated by poor treatment results and compromised physically and emotionally
- Leaves physicians frustrated due to lack of adequate treatment resources and poor outcomes

Zeroing in on the Correct Diagnosis

- In the treatment of CRPS, ensuring a correct diagnosis is key
- Subjective diagnostic criteria and no specific test
- Diagnostic tests are disappointing – a negative bone scan, for example, doesn't rule out the condition and while an electrodiagnostics may pick up non-specific findings, there are no definitive criteria for a diagnosis
- Your best hope for making the right diagnosis is obtaining a good history and doing a careful physical exam

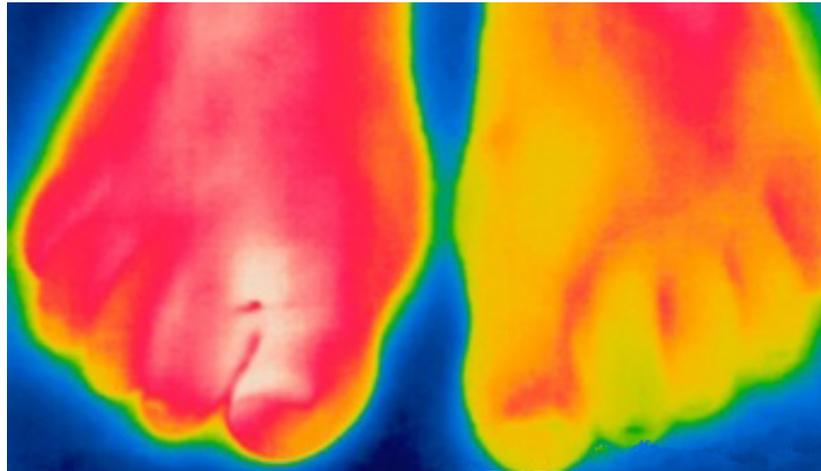
CRPS is **over-diagnosed**. It is a sufficiently vague diagnosis to explain away multiple symptoms and “failure” of treatment. Even more complex when litigation is involved: does the injured worker have a problem, or **do they wish to have a problem** when there is none?¹

Diagnostic Tests

- Triple phase bone scan – consider, but know that it isn't a specific test (19% at best) but is sensitive (96%) early in the condition.
- Diagnostic (and therapeutic) sympathetic blockade – consider.
- Electrodiagnostic tests – to rule out other nerve-related disorders.
- MRI/CT/X-ray to rule out other orthopedic disorders. While not diagnostic, an x-ray showing periarticular osteopenia is significant.
- Thermogram.
- Autonomic testing.

Diagnosis

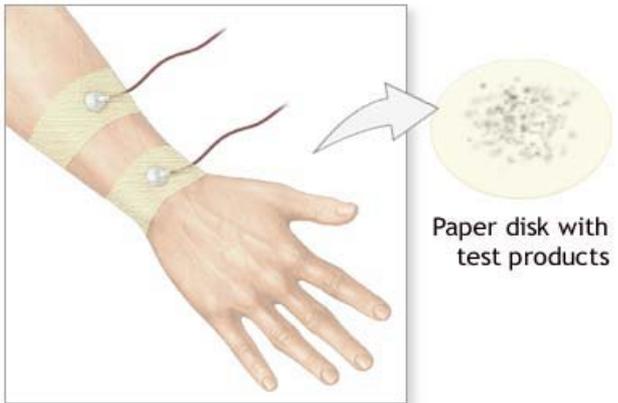
- Thermography—Acclimatize to room at 61-68 degrees Fahrenheit for 20 minutes, then take baseline infrared images. May include 5 minute cold water immersion of unaffected limb as second step. Must avoid nicotine, caffeine, skin lotions, and physical therapy for 3-4 days before test.



Diagnosis

Sweat testing

- Bone Scan/Xrays



Positive and negative electrodes applied

Paper disk with test products

ADAM.



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How the CRPS pain cycle is perpetuated:

In addition to peripheral changes, central nervous system reorganization, altered central processing, and psychosocial factors contribute to the experience of pain.

- Pain causes structural and functional changes in the injured worker's CNS which can amplify and maintain the chronic pain state
- Other factors also play a role in the maintenance and experience of pain and disability; these factors need to be addressed in order to achieve successful outcomes.
- Psychological and social factors can play a more prominent role than biological factors

Treatment

- “The treatment of CRPS is multidisciplinary and aims to educate about the condition, sustain or restore limb function, reduce pain and provide psychological intervention.”¹
- Requires careful selection of treatments for best outcomes – this can include medications, interventions, rehabilitation therapies and psychological treatment.
- Treatment frequently requires a coordinated approach.
- Single-modality treatments likely to be met with treatment failure.
- Goal-oriented treatment is necessary, and the injured worker’s goals need to involve more than just being pain-free.

Setting expectations starts at the first visit.

1. Goebel A. Complex Regional Pain Syndrome in Adults. Rheumatology 2011;50:1739-1750

Best Practices for Treatment

- The practice of surgical and chemical sympathectomy for neuropathic pain and CRPS is based on very little high quality evidence.¹
- Scarcity of published evidence to support the use of local anaesthetic sympathetic blockade for CRPS.²
- Dorsal column stimulators: The (only) large RCT found a response rate of 50% for >50% pain relief in injured workers with >6 months, disease duration. Limb function did not improve. With time, the SCS effect slowly diminishes; SCS results did not exceed those in the physical therapy control group from 3 years after implantation.³
- Surgery to the affected limb is rarely indicated. Any temptation to amputate should be strongly resisted.⁴
- Surgical release of finger contractures has not been successful and has at best a 50% improvement.⁵

1. Cochrane Database Syst Rev. 2013 Sep 2;9. 2. Cochrane Database Syst Rev. 2013 Aug 19; 8. 3. Kemler et al., 2008; 4. Dielssenn et al. 1995; 5. Patterson et al., 2011.

Treatment-Medications

- TCA's for sleep hygiene improvements
- Anticonvulsants (Gabapentin, Lyrica, Topamax, Tegretol)
- Antidepressants (Lexapro, Cymbalta, Savella, Effexor)
- NSAIDS
- Opiates
- Corticosteroids
- Anti-hypertensives (Clonidine, Propranolol, Doxazosin)
- Na Channel blockers (Procainamide, Quinidine, Lidocaine)
- Calcium Channel Blockers (Procardia, Norvasc)
- NMDA receptor antagonists (amantadine, DM, Ketamine)
- Topicals—Lidocaine/DMSO/Ketamine/compounded formulas

Treatment Options

- Opioids (oral/intrathecal/transdermal): A big part of the problem because it's such a small part of the solution; rarely improves function
- Ketamine infusions, compound topical agents
- Rehabilitation: emphasizes normalizing movement patterns, restoring range of motion of affected limb, normalizing sympathetic tone of limb, desensitization, gradually progressing from gentle therapies to intensive rehabilitation targeted at addressing injured worker's emotional, physical and vocational needs
- Treatment modalities: graded motor imagery, left/right discrimination, mirrorbox therapy



Treatment- Conservative

- PT and OT: Hydrotherapy, Myofascial Release, Edema Management, ROM, desensitization, ADL and mobility training, electrostimulation
- Weight Bearing Exercises: Stress loading and Carrying exercises
- Muscle strengthening and cardiovascular conditioning
- Body Awareness, PNF, Feldenkrais
- Graded Motor Imagery and Mirror box therapy
- Recreational therapy
- Vocational Rehab therapy

Treatment- Conservative

- Psychotherapy—Cognitive-Behavioral therapy/Somatic Experiencing/Biofeedback, patient and family education, evaluation and treatment of comorbid psychiatric diagnoses
- Biofeedback/Meditation/Stress Management
- HBO
- Acupuncture
- Nutrition/life-style modifications
- Functional Restoration Programs/Cardiovascular conditioning

Comprehensive Pain Programs: When Are They Warranted?

- It can be time-consuming and requires skilled specialists in the treatment of chronic pain to identify the disability markers delaying recovery, but it is necessary for identifying the injured workers who are failing traditional medical care, which is frequently in the vein of the biomedical model. Avoid unnecessary surgical care.
- Identify the insult and try to eradicate the pain? All injured workers seek this. Works well for many medical illnesses but not CRPS and certainly not chronic pain.
- Without identifying these factors, some of these injured workers can continue to receive aggressive interventional treatments (such as repeated blocks and spinal cord stimulators) and medication management, including opioids, that serve to amplify their pain and disability.

From the Archives: Crush Injury

- 31-year-old man with crush injury to right foot (Lisfranc injury), compartment syndrome, severed peroneal nerve, severe ankle displacement, crushed heel and tibia fracture. s/p 12-13 surgeries.
- Surgeries complicated by osteomyelitis. Pain levels 5-8/10 in right lower leg and right ankle. Uses walking stick constantly. Daily stumbles and falls a few times a month. Presented with altered gait pattern, moderately high levels of pain, high opioid use, difficulty weightbearing on right foot.
- Prior treatment: More than 100 visits of PT, aquatic therapy, massage, psych counseling and treatment for PTSD and depression.
- Had done some desensitization in PT and his home exercise program.
- Recommended pain program, tx with GMI, desensitization and mirror box therapy. Focus to be on strengthening, conditioning, working on ROM, gait training, body mechanics, tolerances for ADLs, endurance and allowing him to return to an appropriate level of work.
- Meds: Prazosin 5 mg qhs, Gabapentin 1200 mg tid, Fentanyl 50 ug/hr q 3 days, Amitriptyline 100 mg qhs, Zoloft 150 mg qd, Methocarbamol, Tylenol, Naprosyn.

Treatment Outcomes

	Pre-treatment	Post-treatment
Pain	5-8/10	3-4/10
Standing tolerance	15 min	60 mins
Lifting capacities	20 lbs	50 lbs
Body mechanics	64%	100%
SF-36	50	85
Pain catastrophizing scale	10	5

- Meds at discharge - Prazosin 5 mg qhs, gabapentin 1200 mg tid

Case Study



Summing it Up

Clinical interventions.

- Correct diagnosis
- Setting treatment expectations
- The failure of the biomedical model
- Consider interdisciplinary treatment early
- Focus on early reactivation
- Caution with opioids
- Consider psychological treatment if there are significant comorbidities
- Invasive treatment should be restricted to selected cases and should only be offered in specialized centers

CRPS treatment outcome is not as poor as commonly assumed. Whether there is return to pre-injury QOL is frequently dependent on the above factors, as well as often dependent on injured worker's personal factors.