

Complex Regional Pain Syndrome: New Hope After a Decade of Dispelling Myths

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Complex Regional Pain Syndrome (CRPS) is a perplexing condition that has been relatively ignored and misunderstood by the medical community because it is so unusual. Perhaps the confusion that is invoked by this condition is precisely due to its atypical clinical presentation: the pain in CRPS patients does not follow a pattern expected in painful neurologic conditions, the affected body part changes color and temperature quite dramatically, and patients often display protective behavior that looks odd to a practitioner. Furthermore, CRPS often may result from a work-related injury and thus may carry suspicion of an ulterior financial motive—although this is rarely, if ever, the case. And lastly, often the CRPS patient has a comorbid psychiatric condition. The net result has been a tendency among many in the medical community to keep CRPS patients at arm’s length, ultimately making it even more difficult for these patients to receive appropriate therapy.

Fortunately, over the past decade an international group of research scientists and clinicians, who are dedicated to advancing our understanding and treatment of this difficult condition, have made great strides. Although there is still no cure or complete understanding of the pathophysiology underlying CRPS, most patients can be helped by educated pain practitioners who are able to alleviate their CRPS patients’ pain and improve function and quality of life with the proper care. This short review article will attempt to dispel old myths, summarize advances in our understanding of CRPS, and describe promising new approaches to therapy.

What Is CRPS?

Over the past decade, a great deal has been published in medical scientific peer-reviewed journals regarding CRPS (“reflex sympathetic dystrophy” and “causalgia”), documenting it as a true biomedical clinical disorder with underlying neurological pathology in both the peripheral and central nervous systems. Numerous attempts have been made to identify common causes and features to serve as a basis for effective

treatment. International pain experts have questioned many of the previously long-held medical assumptions regarding this condition by performing research to test old hypotheses. Their healthy skepticism has resulted in exposing most of these old medical “tenets” as myths or half-truths. CRPS is at last being viewed from a data-driven scientific and clinical perspective ^{1,2}.

A crucial part of this effort has been the attempt by the International Association for the Study of Pain (IASP) to more accurately define this medical condition, now called “Complex Regional Pain Syndrome” (CRPS), and especially to differentiate it from other conditions involving nerve pain ². The new IASP diagnostic criteria recognize two syndromes: CRPS I and CRPS II [Table 1]. Both are conditions in which pain is most often severe and the area affected is characterized by skin sensitivity, abnormal color changes, temperature changes, and sweating. Not all patients have all these symptoms continuously, but they must always have more than just pain and skin sensitivity (allodynia and/or hyperalgesia), which are common among many neuropathic pain conditions. CRPS II (previously called causalgia) differs from CRPS I (or RSD) in being the result of identifiable nerve injury; otherwise, they are the same symptomatically. By accurately defining CRPS, there is a much better chance of finding effective treatments and defining the underlying etiology.

Common Treatment Myths and Half-Truths [Table 2]

Myth 1

One of the major myths regarding treatment of CRPS is that nerve blocks are the key to diagnosis and therapy. Even today, physicians commonly confuse the term “sympathetically maintained pain” (SMP) with CRPS. SMP, by definition, means only that a patient reports pain relief following a sympathetic block; thus, patients with a variety of clinical conditions, such as diabetic neuropathy, can also have SMP.

Furthermore, although nerve blocks may be curative for some patients with CRPS, this is not true in all, and probably most, patients. For many patients, the majority of their pain is thought to be caused by mechanisms independent of the sympathetic nervous system (so-called “sympathetic independent pain”—SIP), and therefore sympathetic nerve blocks are not effective. The authorities have come to acknowledge that the cornerstone

of CRPS treatment is physical and rehabilitation therapy, and not nerve blocks ^{1,2}. It is crucial to remember that the diagnosis of CRPS is a clinical one, based on history and examination findings [Table 1], without regard to response to sympathetic blocks.

Myth 2

A mistaken notion that heightens undue fear and anxiety in CRPS patients is the belief that all CRPS patients will progress through a series of increasingly debilitating stages and that CRPS will spread to other parts of the body. A recent study has shown that there is no one set of stages that every patient goes through, and that the intensity and severity of symptoms/signs do not correlate with duration of CRPS ³. This study also made the important discovery that there appear to be three distinct subgroups of CRPS patients who differ in their grouping of CRPS signs/symptoms: 1) a relatively minor syndrome with vasomotor signs predominating, 2) a relatively limited syndrome with neuropathic pain/sensory abnormalities predominating, and 3) a florid CRPS. Although CRPS may indeed spread, this does not occur in every patient. Moreover, “spreading” of symptoms is often misdiagnosed as progressing CRPS. Instead, what often happens is that disuse or misuse of the affected limb leads to secondary myofascial problems, which then can become another independent source and site of symptoms.

Myth 3

Related to Myth 2 is the erroneous belief that therapy will be unsuccessful unless started early in the course of CRPS. Although it is definitely important to receive treatment as early as possible, patients should not be viewed as hopeless if their CRPS has remained undiagnosed or poorly treated for 5 or even 10 years. Based on authorities’ experience, patients with CRPS can and do respond to a variety of therapies even when they have had the condition for many years ¹.

Myth 4

Perhaps the most pervasive, disturbing, and damaging myth is that CRPS is a psychological disorder and is “all in the patient’s head.” Unfortunately, this tall tale had been perpetuated by many prominent neurologists up until the past few years, causing

undue pain and suffering, as well as assisting the medical-legal-workers compensation systems in denying CRPS patients' right to appropriate (paid-for) healthcare and insurance benefits. To some extent, this misguided belief probably reflects the unusual nature of CRPS as mentioned earlier. Also, like many chronic pain patients, CRPS patients do often develop secondary psychological conditions, including depression, anxiety, or post-traumatic stress disorder (PTSD), as a result of the effect severe pain has on their lives, but not as a cause of the condition^{1,2,4}. It is confirmed by scientific data that CRPS is not a psychiatric condition.

What Causes CRPS?

CRPS is an underlying pain condition that is caused by abnormality in the nervous system, although standard neurological tests are frequently normal (except in CRPS II). Recent animal models for nerve pain have shown that animals suffering a nerve injury can display characteristics similar to humans with CRPS, including sensitivity to touch and changes in temperature and color, as well as “mirror” symptoms, all of which have been found to have an underlying neuropathological cause.

Following injury, the body undergoes a series of physiologic responses designed to heal the damage, including an inflammatory response that results in changes in the area, such as redness, warmth, and swelling. This response is accompanied by changes in the nervous system, which registers pain sensations in the surrounding area, and results in skin sensitivity, allodynia, and hyperalgesia. In effect, many of the signs and symptoms that patients with CRPS experience are part of the normal healing process. These responses usually cease after a short period of time but in CRPS they may continue indefinitely. Thus, one hypothesis is that CRPS represents a disruption of the healing process¹, although it is not known how pain and other CRPS symptoms are maintained over months and even years.

Over the past few years, scientific studies performed with CRPS patients have strongly suggested that brain pathologic changes may be underlying some patients' symptoms, which are likely reversible. A recent study demonstrated that CRPS patients had shrinkage of their somatosensory cortex contralateral to the affected limb, which was reversed with treatment that improved their symptoms⁵.

Is There a Predisposition to Getting CRPS?

To date, there is no known predisposing risk factor for developing CRPS. No psychological profile has been identified that predisposes one to developing CRPS, nor have any data been published that have found a genetic link^{1,6,7}. However, there is evidence suggesting that increased stress at the time of the inciting injury may be a risk factor^{1,6,7}.

Approach to Treatment

Unfortunately, there is no “magic bullet” for patients with CRPS. When a CRPS patient presents for treatment, most authorities generally still recommend a sympathetic nerve block to assess whether the patient has SMP (or SIP). If the patient is found to have SMP, there is a possibility that a series of these blocks may bring significant relief and for a minority of patients may be curative. However, patients and physicians should be warned not to be disappointed if a trial of 1 or 2 nerve blocks indicates that this therapy does not work for them. Each patient is different in terms of response to nerve blocks and medications. Although no treatment has been shown to help all patients with CRPS, the good news is that there is a long list of treatments that have been shown to ameliorate the pain and improve the quality of life for many patients.

It is the responsibility of each pain provider to become familiar with the wide range of treatments reported to help patients with CRPS, not just perform invasive procedures, which will benefit few patients. Also critical in successfully treating CRPS is regular contact among all of the patient’s treating healthcare providers so that their efforts can be coordinated.

Physiotherapy

A central, if not the key, goal of therapy is to get the painful limb moving to restore normative function^{1,2,7}. Methods for accomplishing this goal consist of everything from restoring range of motion, slowly increasing tolerance for daily activities

such as walking and sitting, and reducing sensitivity to clothing and other objects in the environment. Defined PT and OT techniques that have been used successfully include desensitization, stress loading, and a slowly progressive program of active exercise.

Unquestionably, there will be times when patients will not want to move, and other times when they will want to move too much. The key is to have the patient maintain a systematic, long-term, structured program where slow and gradual gains are made on a weekly basis, both in the gym and at home.

Psychotherapy

Psychological assessment and counseling is important, not because psychological factors cause CRPS, but because, like all chronic pain conditions, CRPS often has profound psychological effects on patients and their families. CRPS patients may suffer from major depression, anxiety, or post-traumatic stress disorder, all of which tend to heighten the perception of pain and make rehabilitation efforts more difficult^{1, 2, 7}.

Patients who are not optimally treated for these psychological conditions simultaneously with their pain will not obtain optimal benefit from the overall treatment plan.

Pharmacotherapy

Because there is no known cure for CRPS, pharmacotherapy is aimed at relieving painful symptoms in order to facilitate patient participation in rehabilitation therapy and, over time, a return to as much normal activity as possible. Medications should be tried one at a time, slowly but aggressively, making changes (increasing or decreasing doses, or changing medication) over the course of a few days or a week, if necessary, until the right agent or combination of agents is found that provides the optimal degree of pain relief with the most tolerable side effects. It is crucial to perform one medication change at a time so that the provider can ascribe improvement or side effects to the correct drug. As in treating any chronic pain condition, no one drug is effective in every patient, and each patient differs in terms of response and dosage required. However, with a persistent, systematic approach, most CRPS patients can eventually find a medication or group of medicines that provides meaningful pain relief^{1, 2, 7}.

Although randomized trials are scarce in CRPS (according to published reports and expert opinion), it is recommended that medication management be based on 3 classes of drugs [Table 2]; (these recommendations also generally comply with the recent clinical recommendations published for the treatment of neuropathic pain conditions ⁸:

1. Topical drugs (targeted peripheral analgesics), by definition, do not deliver meaningful amounts of medication to the bloodstream, but act locally on the painful nerves, skin, and muscles. Therefore, this class of drugs rarely, if ever, produces any systemic side effects. Currently, the only FDA-approved topical analgesic is the lidocaine patch 5% (Lidoderm[®]), which is indicated for another neuropathic pain condition, postherpetic neuralgia. Several publications have shown it to be potentially efficacious in other painful nerve conditions, including CRPS and diabetic neuropathy, as well as inflammatory conditions, such as osteoarthritis ⁹. A case series has shown a compounded form of the NDMA-antagonist, ketamine, to be of potential effectiveness ¹⁰, although caution should always be used when using non-FDA formulations.

2. Anticonvulsant seizure medications are now first-line therapies to treat a variety of neuropathic pain conditions. Although many of these agents tend to have intolerable side effects, gabapentin (Neurontin[®]) and pregabalin (Lyrica[®]) are among those that may be better tolerated.

3. Opioid therapy has also become a mainstay in the treatment of a variety of chronic pain conditions, including neuropathic pain states. Drugs in this class include oxycodone ER, oxymorphone ER, morphine ER, and the transdermal fentanyl patch. Although addiction is believed to be rare in properly treated chronic pain patients, practitioners should be aware of the behaviors that may reflect misuse and the tools that may assist in such evaluation ¹¹.

Drugs in Development

Although definitive data have not been published, several possible exciting new therapies may be available over the next few years. Thalidomide is currently being studied, based on the positive experience of some patients ¹². Also, recent reports have shown promise for controlled intravenous infusions of ketamine ¹³.

Conclusion

Research performed over the past decade has brought much enlightenment to our understanding of CRPS and has helped to dispel many myths that had resulted in further pain and suffering among CRPS patients. As such, the next decade promises more progress, thanks to the many dedicated researchers and clinicians worldwide. A new, revised *CRPS Treatment Guidelines* is currently being written by CRPS experts, led by Dr. Norman Harden, and should be read by all pain practitioners when published. In addition, the pharmaceutical industry is very much involved in searching for new therapies to treat CRPS and other chronic neuropathic pain conditions.

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