COMPLEX REGIONAL PAIN SYNDROME: TREATMENT GUIDELINES

Edited by R. Norman Harden, MD

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PREFACE

"Consider, too, that in publicizing RSD, we generally focus on the pain, not the disabilities that come with it—the legs and hands that no longer work, the bones that become osteoporotic, the joints that become locked, the muscles that become spastic…There is an awful lot we leave out—how a productive member of society can become too disabled to work or take care of her children. We don't discuss the tremendous personal losses—families, friends, jobs—that RSD wreaks…"[1]

So wrote Linda Lang, author, RSDSA board member, and a woman who has suffered with RSD for nearly 20 years. Linda is not alone—hundreds of thousands of individuals who are currently suffering with the burning, sharp, aching pain and the potential disability of RSD, now known as Complex Regional Pain Syndrome Type 1 (CRPS), understand the losses that accompany the horrific pain.

Although measuring pain is subjective, the losses are measurable, and often substantial. One prospective study of 829 patients with CRPS in the Netherlands reported that the syndrome is a major cause of disability because only one in five patients was fully able to resume prior activities.[2] A recent web-based epidemiological survey of CRPS conducted by RSDSA, in conjunction with the Johns Hopkins School of Medicine, corroborated the findings of Dr. Veldman et al that CRPS results in a high incidence of disability from work, continuing intense pain, sleep disturbance, and suicidal ideation.[3]

CRPS can be a very difficult syndrome to treat, especially if treatment is offered piecemeal rather than in an interdisciplinary fashion as recommended. Our goal in writing these guidelines is to make sure that those individuals suffering with CRPS receive the proper diagnosis and appropriate treatment. Through education, we hope to minimize patient losses as much as we possibly can. Dr. Norman Harden, the contributing authors, and our review editors have attempted to write these guidelines based chiefly on evidence-based medicine. We dedicate these guidelines to people with CRPS, their families and support people, and the medical professionals who accept the challenge of treating this poorly understood, perplexing syndrome.

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June 2006

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INTRODUCTION AND DIAGNOSTIC CONSIDERATIONS

R. Norman Harden, MD, and Stephen Bruehl, PhD

INTRODUCTION

Among the many names that Complex Regional Pain Syndrome (CRPS) has been called, Reflex Sympathetic Dystrophy (RSD) and causalgia are the most well known. The several names for CRPS stem from the many nonstandardized, idiosyncratic diagnostic schemes with which it has been diagnosed throughout the past century and a half.[1-4] In 1851, Claude Bernard (1813-1878) was the first to identify a pain syndrome that was linked to sympathetic nervous system dysfunction. Later, a student of Bernard's, Silas Weir-Mitchell (1829-1914), employed the term "causalgia" to describe the pain he diagnosed in American Civil War union veterans (Greek: kausos=heat, algos=pain). Evans first coined the term "reflex sympathetic dystrophy" (RSD).[5] Though "RSD" became the most common name to describe this medical condition in the 20th century, this name is problematic for many reasons: If a true "reflex" is indeed involved, it is complicated/multisynaptic and not fully characterized; it has since been shown that the assumed "sympathetic"/autonomic changes may not be a constant or causative pain component, and furthermore may not be physiologically involved throughout the entire course of the condition in every patient; and actual "dystrophy" is present in perhaps only 15% of cases. The historical lack of agreement regarding standardized nosology and diagnostic criteria for CRPS/RSD has hindered medical and scientific progress in many ways, including a lack of comparison studies of diagnosis and treatment of the disorder, and has delayed progress in identifying optimal treatments and treatment sequences for its sufferers.

Primary attempts to outline diagnostic criteria for this syndrome incorporated anecdotal clinical syntheses of signs and symptoms derived from experience, such as those by Bonica,[1] while attempts to identify formal criteria only appeared decades later.[2, 4, 6] Although commendable, the multitude of efforts added to the increasing literature of anecdotal, inconsistent diagnostic schemes. For many decades, this ongoing lack of general agreement over the characterization of the syndrome continued to encumber both research and other endeavors that were undertaken in order to improve management of the disorder. To reverse this trend of diagnostic chaos, more recent efforts to formally define the syndrome have taken place at consensus workshops. The Schloss Rettershof conference in 1988[7] and the more definitive Orlando conference in 1994[8,9] were international consensus efforts held to create scientifically validated diagnostic criteria designed to be inclusive, sensitive, and broad. The consequent taxonomy and criteria were adopted by the Committee for Classification of Chronic Pain of the International Association for the Study of Pain (IASP).[10] These materials have greatly aided the understanding of the syndrome (see Table 1), created the potential for improved clinical communication, and helped engender homogeneity within and across research samples around the world.[9]

The criteria that emerged from the Orlando conference were necessary and important, yet experience gained from developing diagnostic criteria for headache and psychiatric disorders (other clinically based diagnostic schema) indicates the necessity of validating and modifying such preliminary consensus-based criteria through systematic validation research.[11] Consensus-derived criteria that are not empirically validated may lead to over- or underdiagnosis

of the syndrome and thus may reduce the ability to provide timely and optimal treatment. Because the IASP criteria for CRPS taken from the Orlando conference represent the consensus opinion of only a small group of expert clinicians, they required clinical validation. Additionally, the use of the IASP criteria has been sporadic in the literature since their publication in 1994,[12] and the failure of the majority of researchers in the field to use them has continued to restrict the full and potential benefits of having a common set of criteria.

This chapter will describe empirical/statistical methods for validating the diagnostic criteria for CRPS, discuss the results of the validation studies to date, and, finally, encapsulate the latest international consensus group's action in Budapest, Hungary, which approved and codified these empirically derived criteria as a revision of the Orlando (1994) criteria.

INTERNAL VALIDATION

A closer study of internal validation of the 1996 IASP/CRPS criteria raises many questions concerning the integrity of the internal structure. For example, is the combination of edema, vasomotor, and sudomotor signs and symptoms in a single criterion the best, most efficient grouping (criterion 3 of IASP/CRPS criteria as described in Table 1), or does this diminish diagnostic specificity and/or sensitivity? Additionally, are the CRPS criteria adequately complete, or have pivotal criteria with potential treatment implications been overlooked?[8, 13, 14] Diagnosis and treatment of the syndrome will improve only when such questions are addressed in a scientific manner.

Distinct subgroups of CRPS can be derived from statistical pattern recognition methods such as factor analysis and cluster analysis. Such methods have been used previously for internal validation of headache diagnostic criteria,[15-17] as well as psychiatric diagnostic criteria.[18] Factor analysis is a statistical method that groups coherent, and presumably conceptually linked, variables into subsets (factors) within a dataset. These subsets can then be grouped together statistically (ie, if one sign/symptom in a given factor is present, it is more likely that another sign/symptom in that factor will also be present). Factor analysis can thus provide distinct, statistically derived subgroups of CRPS signs and symptoms (factors) as they present in the clinical setting. Signs and symptoms that group together into the same factor may be reasonably assumed to share some underlying pathophysiology (eg, color and temperature changes are both mediated by vasoconstriction).

Although the consensus-derived Orlando IASP/CRPS criteria suggested that signs and symptoms of CRPS cluster into two subgroups (pain/sensory and vasomotor/sudomotor/edema), internal validation research using factor analysis in a series of 123 patients revealed that characteristics of CRPS actually clustered into four statistically distinct subgroups (see Table 2; also see [19] and [20] for a list of signs and symptoms studied). The Orlando grouping of the statistically distinct vasomotor and sudomotor/edema subsets of signs and symptoms into a single criterion in the IASP taxonomy (criterion 3) was demonstrated to be particularly problematic. Grouping two distinct clusters of signs/symptoms into a single diagnostic criterion lowered the clinical diagnostic threshold, leading to poor specificity and probable overdiagnosis of the disorder.[19, 20]

In addition to the suggested regroupings of signs and symptoms described above, factor analysis identified a fourth statistically distinct subgroup as well, consisting of a number of clinical characteristics not currently reflected in the

Orlando IASP/CRPS diagnostic criteria but often seen in practice. These signs and symptoms have been frequently recognized in the older literature as fundamental features of RSD.[8, 19, 20] The older RSD literature describes various signs of motor dysfunction (eg, dystonia, tremor)[6, 14, 21] and trophic features (eg, changes in hair or nail growth, development of thin, "shiny" skin)[2, 4] as being important clinical features of the syndrome. Factor analysis indicates that these motor/trophic characteristics form a fourth, distinct subset of CRPS signs and symptoms that group/factor together but do not overlap substantially with the three other subgroups described above.[19] The historical, clinical observations of the syndrome coupled with these recent findings indicate that a group of diagnostically relevant signs and symptoms of the disorder were likely omitted from the Orlando criteria.

EXTERNAL VALIDATION

The external validity of the Orlando IASP/CRPS criteria has also been assessed. The external validity of the diagnostic criteria for CRPS measures its ability to distinguish CRPS patients from other neuropathic pain patients (ie, those not involving significant evoked sensory alterations, autonomic component, etc). An ideal diagnostic criteria would make an unambiguous distinction between neuropathic pain patients based upon some clear external reference point or "gold standard,"[22] but without a known pathophysiology for CRPS, such a "gold standard" does not yet exist. Providing evidence for the external validity of the Orlando IASP/CRPS criteria is therefore challenging, but not impossible.[20]

The Orlando criteria themselves can be used as a reference point to test external validity.[20, 23] For this process, a CRPS patient group should be identified using a strict application of the Orlando criteria and then compared to a non-CRPS neuropathic pain group that has been diagnosed using other available diagnostic information (eg, proven, chronic diabetes with ascending symmetrical pain, confirmed by electrodiagnostic studies). It is critical to note that this latter group does not simply consist of patients who fail to meet Orlando criteria, but rather, reflects a non-CRPS diagnosis derived from independent objective criteria. Thus, by using the Orlando IASP/CRPS criteria, which were originally used to define the CRPS group, to distinguish between the two groups of patients, the "deck has been stacked" in favor of being able to discriminate accurately between the CRPS and non-CRPS neuropathic pain patients. If the diagnostic criteria cannot distinguish accurately between CRPS and other clinically distinct neuropathic pain conditions based upon patterns of signs and symptoms, even under such favorable test conditions, the criteria are likely to be of limited utility in research and to the average clinician. A distinct disorder such as diabetic neuropathy will most likely not present a differential diagnostic challenge in clinical practice because of the clear existence of another condition "that would otherwise account for the degree of pain and dysfunction" (see criterion 4, Table 1), but the use of such disorders for testing the discriminative ability of CRPS diagnostic signs and symptoms provides an effective model for examining external validity issues.

RECENT VALIDATION STUDY RESULTS

In a preliminary external validation study, 18 patients meeting Orlando IASP/CRPS criteria and 30 patients with painful diabetic peripheral neuropathy were examined. Initial study results indicated that the use of the IASP/CRPS criteria and decision rules (eg, criterion 3 is satisfied by presence of edema or skin blood flow changes or sweating changes) to make diagnostic decisions could lead to considerable overdiagnosis. If glucose tolerance status were not

known and diagnoses were made solely based on the pattern of signs and symptoms, up to 37% of diabetic neuropathy patients would be misdiagnosed as having CRPS if one used the Orlando IASP/CRPS criteria.[23]

Similar findings were determined in a larger external validation study.[20] The sample consisted of 117 patients meeting IASP/CRPS criteria and 43 neuropathic pain patients with established non-CRPS etiology; these 43 non-CRPS patient diagnoses included diabetic neuropathy, polyneuropathy, post-herpetic neuropathy and radiculopathy. The Orlando criteria and decision rules (eg, "evidence at some time" of edema or color changes or sweating changes satisfy criterion 3) discriminated appreciably between the CRPS and non-CRPS groups. However, closer examination of the results indicated that while diagnostic sensitivity (ie, ability to detect the disorder when it is present) was quite high (.98), specificity (ie, minimizing false positive diagnoses) was very poor (.36), and a positive diagnosis of CRPS was likely to be correct in as few as 40% of cases.

Sensitivity is extremely important in a clinical setting. Yet specificity is also quite important clinically to reduce potential morbidity associated with therapies, such as adverse reactions to medications and unnecessary invasive treatments. When sensitivity is high at the expense of specificity, CRPS may be overdiagnosed and, ultimately, overtreated in a clinical setting. High sensitivity causes the identification of pathophysiologically/mechanistically heterogeneous cohorts for research, potentially contributing to negative results in clinical trials. In order to treat patients adequately, such overdiagnosis must be balanced with the equally undesirable consequences of failing to identify clinically relevant syndromes. Therefore, although the use of the Orlando criteria in an external validation model tends to inflate diagnostic sensitivity, such a model can be useful for testing the effects of modifications to the criteria on specificity and overall diagnostic accuracy.

STATISTICALLY DERIVED REVISION OF CRPS CRITERIA ENDORSED BY THE BUDAPEST CONSENSUS WORKSHOP

A set of research criteria derived from the results of the previously mentioned factor analysis and external validation was developed in order to provide such a test.[19, 20] These adapted criteria grouped all CRPS traits into one of the four statistically derived factors described above (pain/sensation, vasomotor, sudomotor/edema, motor/trophic; see Table 3A). In light of evidence from the Galer et al (1998)[23] and Harden et al (1999)[19] studies, which demonstrated that objective signs on examination and patient-reported symptoms both provide valuable but nonidentical data, the adapted research criteria required the incidence of signs and symptoms of CRPS for diagnosis.

A study testing the ability of these proposed criteria to differentiate between CRPS and non-CRPS neuropathic pain groups suggested that a modification of the Orlando IASP/CRPS diagnostic criteria could improve overall diagnostic accuracy.[19, 20] Results showed that employing a decision rule requiring two of four sign categories and four of four symptom categories for a positive diagnosis resulted in a sensitivity of .70 and a specificity of .94. Of all those tested, this decision rule resulted in the highest probability of accurate diagnosis for both CRPS and non-CRPS patients (approximately 80% and 90% accuracy, respectively), even when a relatively low occurrence rate for CRPS was assumed.[19, 20] In 2004, the Budapest IASP consensus group deemed this high level of specificity advantageous in a research context and subsequently adopted the rules as components of the Proposed *Research* Criteria (Table 3B).

The significance of appropriate decision rules in the criteria is underlined by the fact that the use of these modified criteria, requiring two of four sign categories but only two of four symptom categories to be positive, resulted in a sensitivity of .94, but a specificity of only .36,[20] the same as the lack of specificity displayed by the Orlando IASP/CRPS criteria. This emphasizes the fact that both sensitivity and specificity can be strongly distorted by the decision rules acted upon.[19, 20] Decision rules must be determined according to purpose: identification of stringent research samples (minimizing false positives) versus identification of the highest number of CRPS patients possible (minimizing false negatives). The consensus panel therefore implemented a different set of decision rules for Proposed *Clinical* Criteria (see Table 3A), requiring two of four sign categories and three of four symptom categories to be positive. This ostensibly minor adjustment (merely requiring three rather than four symptoms) resulted in a sensitivity of .85 and a specificity of .69, which represented a good compromise in identifying as many patients as possible at an acceptably accurate rate in the clinical context (see Tables 3A and 4). In response to the consensus group's concern with the approximately 15% of patients previously diagnosed with CRPS, a third diagnostic subtype called CRPS-Not Otherwise Specified (NOS) was created that would capture those patients who did not meet the new clinical criteria, but whose signs and symptoms could not be better elucidated by any other diagnosis (see Table 5). This subtype was a practical compromise and may not be necessary in the long term as research provides specific information about mechanism(s), and thus diagnostic techniques.

CRPS STAGES? CRPS SUBTYPES?

Is CRPS a uniform phenomenon across individuals, or are there distinct subtypes or stages of the syndrome? This issue, addressing whether or not patient presentations (ie, the overall pattern of CRPS signs and symptoms) tend to be similar across individuals, requires validation. Historically, three progressive stages of CRPS have been cited as important in identifying and treating the syndrome (eg, [1, 24, 25]), but the existence of such sequential stages has been traditional lore, unsubstantiated theory based on certain authors' experience rather than an outcome of empirical scientific study. This hypothesized staging can be tested by using cluster analysis to bracket CRPS patients into three subgroups delineated according to similarity of signs and symptoms. If the theorized stages exist, the subsequent statistically derived patient subgroups should vary considerably with regard to pain duration (ie, predictable progress of CRPS through the three stages should take place); furthermore, the clinical presentation within the three subgroups should correspond to the three assumed stages of CRPS (best described in Reference 1).

One hundred thirteen patients meeting IASP criteria for CRPS went through standardized history and physical examinations designed to evaluate CRPS signs and symptoms in the four previously described factor analytically derived domains.[26] After preliminary assessment, K-Means cluster analysis was employed to develop three relatively homogeneous CRPS patient subgroups based on correspondence of sign/symptom patterns in these spheres. The resultant CRPS patient subgroups did not vary considerably in pain duration as might be predicted in a sequential staging model. Moreover, the most frequent signs and symptoms in each of the three patient clusters did not correspond closely to those that should have been anticipated based on published descriptions of the three stages.[1] Contrary to the historic lore of time-sequenced progressive stages, the scientific analysis (ie, cluster analysis) suggested the possible existence of three statistically distinct CRPS subtypes: 1) a relatively limited syndrome with vasomotor signs predominating, 2) a relatively limited syndrome with neuropathic pain/sensory abnormalities predominating, and 3) a florid CRPS syndrome similar to "classic RSD" descriptions. Importantly, despite having the briefest pain

duration of the three groups, Subtype 3 displayed the greatest levels of motor/trophic signs and possible disuse-related changes (osteopenia) on bone scan. EMG/NCV testing indicated that Subtype 2 may be synonymous with CRPS-Type 2 (causalgia). Even though this study did not address the individual patterns of temperature changes detected in CRPS patients (eg, warm versus cold), research suggests that these patterns may vary over time.[27] It would therefore be constructive to see if future work examines whether or not these specific patterns relate to the patient subtypes identified.

In conclusion, these preliminary results argue against the historical three *sequential* stages of CRPS.[28-30] Future application of comparable analytic methods to the complexities of CRPS may permit the identification of discrete CRPS subgroups with the goal of being able to target treatment more effectively.

In 2004, the Budapest consensus group considered this information too preliminary to warrant the adoption of these subtypes (or any other scheme) into the formal diagnostic criteria. However, the consensus group did address the old CRPS subtypes that were reported at the Orlando conference and in the IASP criteria (1994). There was a broad consensus that problems do exist with creating a division between CRPS-Type I (see Table 1: without distinct major nerve damage, most like the old RSD) and Type II (see Table 1: with major nerve damage, most like the old causalgia). The consensus group found these divisions to contain rather nebulous definitions of what constitutes "major" nerve damage, and they discussed how objective definitions might be more accurately determined. The problem of distinguishing CRPS-Type I vs. Type II is complicated clinically by the fact that the definitive tests of nerve damage, such as EMG, are considered unnecessarily painful (even cruel) to CRPS patients. Moreover, this diagnostic distinction may not have clinical significance or affect the specific therapeutic method used. Despite these limitations, the distinction between these two existing CRPS subtypes was preserved by the Budapest group, and an eventual re-evaluation of this matter was postponed until more data pertaining to its clinical importance become available.

CONCLUSIONS AND CLINICAL IMPLICATIONS

The Orlando IASP/CRPS diagnostic criteria were developed to furnish an objective means of determining whether unidentified pain conditions indicate CRPS (ie, in which significant autonomic dysfunction is present) or some other type of neuropathic pain. Therapy for these two types of conditions may differ, and application of inappropriate (and possibly expensive) treatments due to misdiagnosis may add to unnecessary morbidity and medical costs. Worse still, misdiagnosis may delay more appropriate therapy in some situations. Therefore, the empirically guided modifications described above, which enhance the accuracy of the CRPS diagnostic criteria, should positively affect issues of patient quality-of-life and reduce issues of medical overutilization, side effects, etc. Additionally, such improvements and revisions to the CRPS criteria will aid in more accurately recognizing research candidates and more effectively determining therapeutic outcomes.[13] Yet because the current understanding of the pathophysiology of the syndrome is incomplete, the statistical method described in this chapter remains one of the few existing objective techniques for validating the IASP/CRPS criteria and indicating the direction of the modifications necessary to optimize their clinical and research value.

Even though the validation methodology described tends to overstate diagnostic sensitivity, results thus far do suggest that the IASP/Orlando diagnostic criteria are acceptably sensitive (ie, they rarely miss a case of actual

CRPS). However, both internal and external validation research indicates a tendency towards overdiagnosis with these Orlando criteria.[19, 20, 23] This overdiagnosis may result from the grouping of discrete elements of the syndrome (vasomotor changes and sudomotor changes/edema) into the same diagnostic criterion. The information also suggests that failure to include motor/trophic signs and symptoms in the current criteria could lead to excluding vital information that may aid in discriminating CRPS from other syndromes. The closed-consensus workshop in Budapest adopted and codified the criteria in Table 3, and these criteria are being proposed to the Committee for Classification of Chronic Pain of the IASP for future revisions (the next being the third) of their formal taxonomy and diagnostic criteria for pain states. A trial of these modified research diagnostic criteria suggests that a dramatic reduction of the rate of overdiagnosis is possible despite the fact that such changes also modestly diminish diagnostic sensitivity.[20] The consensus group debated the relative merits of improved specificity at the expense of diagnostic sensitivity, and ultimately adopted two similar sets of criteria differing only in the decision rules employed (summarized in Tables 3A and 3B): one specifically designed for clinical settings, and the other designed for research settings.

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TABLE 1. IASP (ORLANDO) DIAGNOSTIC CRITERIA FOR COMPLEX REGIONAL PAIN SYNDROME

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 some time 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 I: *without* evidence of major nerve damage
Type II: *with* evidence of major nerve damage

(Adapted from [10])

TABLE 2. FACTORS (AND FACTOR LOADINGS) RESULTING FROM PRINCIPAL COMPONENTS FACTOR ANALYSIS OF DIAGNOSTIC AND ASSOCIATED SIGNS AND SYMPTOMS OF CRPS

Factor 1	Factor 2	Factor 3	Factor 4
Hyperalgesia Signs (.75)	Temperature Asymmetry Symptoms (.68)	Edema Signs (.69)	Decreased Range of Motion Signs (.81)
Hyperesthesia Symptoms (.78)	Color Change Signs (.67)	Sweating Asymmetry Signs (.62)	Decreased Range of Motion Symptoms (.77)
Allodynic Signs (.44)	Color Change Symptoms (.52)	Edema Symptoms (.61)	Motor Dysfunction Signs (.77)
			Motor Dysfunction Symptoms (.61)
			Trophic Symptoms (.52)
			Trophic Signs (.51)

Note: Factor loadings can be interpreted as correlations between individual signs/symptoms and the overall factor on which they load.

TABLE 3. REVISED CRPS CRITERIA PROPOSED BY THE BUDAPEST CONSENSUS GROUP

General Features of the Syndrome:

CRPS describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time.

There are two versions of the proposed diagnostic criteria: a clinical version meant to maximize diagnostic sensitivity with adequate specificity, and a research version meant to more equally balance optimal sensitivity and specificity. These proposed criteria are described in Table 3A and Table 3B, respectively.

TABLE 3A. CLINICAL DIAGNOSTIC CRITERIA FOR CRPS

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)
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 deep somatic pressure and/or joint movement)
   Vasomotor: Evidence of temperature asymmetry 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 range of motion 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

*A sign is counted only if it is observed at time of diagnosis.

TABLE 3B. RESEARCH DIAGNOSTIC CRITERIA FOR CRPS

1) Continuing pain, which is disproportionate to any inciting event
2) Must report at least one symptom in *each 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).
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 deep somatic pressure and/or joint movement).
   Vasomotor: Evidence of temperature asymmetry 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 range of motion 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.

*A sign is counted only if observed at time of diagnosis.

TABLE 4. SUMMARY OF SENSITIVITY AND SPECIFICITY OF THE PROPOSED CLINICAL AND RESEARCH CRITERIA

Criterion Type	Symptom Categories Required for Diagnosis	Sign Categories Required for Diagnosis	Sensitivity	Specificity
Clinical	≥ 3	≥ 2	0.85	0.69
Research	= 4	≥ 2	0.70	0.96

TABLE 5. SUBTYPES OF CRPS

CRPS I (old name: Reflex Sympathetic Dystrophy): As defined in Table 3.
CRPS II (old name: Causalgia): Defined as above with electrodiagnostic or other definitive evidence of a major nerve lesion.
CRPS-NOS* (Not Otherwise Specified): Partially meets CRPS criteria; not better explained by any other condition.

*This subtype was added to capture any patients previously diagnosed with CRPS who now did not meet criteria.