Perspective

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The Valencia consensus-based adaptation of the IASP complex regional pain syndrome diagnostic criteria

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The new IASP diagnostic criteria for complex regional pain syndrome (CRPS) (aka "the Budapest Criteria"[3]; **Table 1**) have improved the diagnostic specificity for CRPS while maintaining good sensitivity. Internationally, these criteria are now in common use. The IASP CRPS Special Interest Group convened a workshop of CRPS experts in Valencia/Spain in September 2019 to review perceived ambiguities in the diagnostic text and issues identified in applying these criteria in both the research and clinical contexts. After this review, workshop attendees discussed and reached a consensus regarding adaptations to the diagnostic taxonomy text. This process resulted in pragmatic updates to CRPS assessment instructions and the associated text in the IASP taxonomy. The wording of the diagnostic criteria themselves was not altered so as to avoid invalidating the criteria.

The results of this meeting were also used as a justification to update the new *ICD-11* text regarding CRPS and its diagnosis. This focus on incorporating changes into the *ICD-11* was triggered by the current absence of plans to further update the existing CRPS IASP taxonomy. A consensus proposal was sent to WHO for amending *ICD-11* CRPS-related text.[5] WHO has already accepted some adaptations (marked with # below). Here, we summarise all the proposed changes. The proposed wording of all new text for CRPS in the *ICD-11* development version is attached in the web appendix (Online appendix, available at http://links.lww.com/PAIN/B358).

Changes concern 3 areas: (a) diagnostic parenting under *ICD-11*, (b) CRPS subtypes, and (c) the diagnostic procedure.

(a) Diagnostic parenting under *ICD-11*:

The current first parent classification of CRPS in the *ICD-11* is "focal or segmental autonomic disorder" (*ICD-11* BD8A). We consider this classification to be a mistake based on the historic misunderstanding of CRPS as primarily an autonomic disorder. The past 3 decades of CRPS experimental and clinical research clearly demonstrate that this is not the case. We therefore have proposed that the correct parent is "chronic primary pain." This proposal is also supported by the American Autonomic Society.

(b) CRPS subtypes:

(i) CRPS II as defined in the IASP criteria is associated with discrete peripheral nerve damage as indicated by neurological examination, electrodiagnostic testing, or other quasi-objective testing. We now clarify that the diagnostic signs of CRPS II must extend beyond any identified injured nerve territory. Nerve lesion itself may cause separate CRPS-concomitant symptoms and signs, including neuropathic pain, paraesthesias, numbness, and autonomic dysfunction restricted to the injured nerve territory. CRPS II should therefore not be classed as a neuropathic pain condition in accordance with current criteria #.[4] Diagnostic signs of CRPS I (without discrete nerve damage) and II are identical. The clinical relevance and implications of subgrouping CRPS into these 2 subtypes remain unclear at present.#

(ii) We have introduced a third CRPS subtype and have also modified the description of the current diagnostic label CRPS Not Otherwise Specified (NOS) to minimise any confusion with using this latter term. Patients previously documented as having fully met CRPS criteria (either CRPS I or CRPS II, **Table 1**) but who currently display CRPS features insufficient to fully meet the diagnostic criteria should be classified into the new CRPS subtype, "*CRPS with Remission of Some Features*." These patients should not be classified as having CRPS NOS. Notably, a reduction in the number of CRPS diagnostic signs and

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painjournalonline.com).

PAIN 162 (2021) 2346–2348

http://dx.doi.org/10.1097/j.pain.0000000000002245

Table 1

New IASP diagnostic criteria for complex regional pain syndrome ("Budapest criteria"[2]) (A–D must apply).

A. The patient has continuing pain which is disproportionate to any inciting event	□
B. The patient reports at least one symptom in 3 or more of the categories	□
C. The patient displays at least one sign in 2 or more of the categories	□
D. No other diagnosis can better explain the signs and symptoms	□

Category		Symptom (the patient reports a problem)	Sign (you can see or feel a problem on examination)
1 "Sensory"	*Allodynia* (to light touch/brush stoke and/or temperature sensation and/or deep somatic pressure and/or joint movement), and/or *hyperalgesia* (to pinprick)	Reported hyperesthesia also qualifies as a symptom □	□
2 "Vasomotor"	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	□	□
3 "Sudomotor/ oedema"	Oedema and/or sweating changes and/or sweating asymmetry	□	□
4 "Motor/trophic"	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)	□	□

Adapted from https://www.rcplondon.ac.uk/guidelines-policy/complex-regional-pain-syndrome-adults with permission.

symptoms does not necessarily constitute an improvement in the lived experience of CRPS; these patients may not have improved pain nor are they usually free of all CRPS-related signs and symptoms. *CRPS with Remission of Some Features* is a third formal subtype of CRPS, which by necessity overlaps with either CRPS I or II. At what point CRPS changes from being an ongoing condition potentially requiring continued clinical management (ie, *CRPS with Remission of Some Features*) to being considered resolved is a topic that will need to be addressed in future research.

(iii) The term "CRPS-NOS" in the current IASP criteria has been retained exclusively for application to patients who have *never* been documented to fulfil the new IASP CRPS criteria (**Table 1**). That is, they now display some but not all features of CRPS required for formal diagnosis, *and no other diagnosis better explains* the clinical features.

(iv) Warm/cold CRPS and early/persistent CRPS are overlapping presentations that are clinically observed. The group did not consider there to be sufficient evidence yet to create formal CRPS subgroups according to these features. However, there was consensus that research and clinical reports should include this information when describing individual patients, study inclusion criteria, or research participants (clinical experience and research suggest that a substantial proportion of individuals who develop acute CRPS improve or resolve, with a smaller subgroup that fails to substantially improve even with standard care. This transition of CRPS to a more prolonged and difficult to manage condition seems to occur during the first 12-18 months after onset, although there is no widely accepted demarcation point for this distinction. The word "persistent" is used here as a descriptive term for this subgroup of prolonged and intractable CRPS. Use of the alternative term "chronic" is preferred by some CRPS experts. However, we note that the term "chronic" is also broadly used across all pain conditions to refer to pain lasting more than 3 months after tissue injury to distinguish it from "acute" pain. To avoid incorrect implications of the word 'chronic' to be understood as a >3 months' pain duration in patients with CRPS, the word "persistent" is used to refer to such prolonged CRPS. For clarity, 'persistent' does not necessarily indicate the condition will persist indefinitely—a minority of patients with persistent CRPS will naturally improve).#

(c) The diagnostic procedure

ICD-11 includes additional text to clarify diagnostic terms and procedures. The purpose of that text, pragmatic clarification of the diagnostic process, bears resemblance to that of the IASP taxonomy and associated text (https://www.iasp-pain.org/files/Content/ContentFolders/Publications2/ClassificationofChronicPain/Part_II-A.pdf), which is not currently being updated. This *ICD-11* supplemental text has now been updated for CRPS. The following key points are now all implemented (except viii):

(i) All patients should be asked systematically about all symptoms listed in the criteria at each formal diagnostic evaluation, even if they have not previously reported certain symptoms. This is recommended because CRPS signs and symptoms are clinically observed to fluctuate over time.#

(ii) *Clarification* of *the terms "asymmetry" and "changes"* as used in the current IASP CRPS criteria (**Table 1**): For unilateral CRPS, assess *asymmetry* by comparing the affected side to the unaffected side. For (much rarer) bilateral and symmetrical CRPS, assess *changes* in the affected limbs relative to an unaffected limb in the patient or to the limbs of a typical healthy individual. Asymmetry is based on clinical judgment only, rather than any prespecified criteria.#

(iii) For evaluating possible spreading of CRPS beyond a single limb, *the full diagnostic criteria must be applied to each limb individually.* True spreading of CRPS is defined as CRPS that meets full new IASP/ICD-11 diagnostic criteria (**Table 1**) for multiple limbs—extension of pain alone to other limbs, which is not unusual, in the absence of other CRPS features is not formally considered to be spreading CRPS.#

(iv) *Hyperalgesia* (note that other definitions of hyperalgesia and allodynia exist for use in other chronic pain conditions)[4] is a clinical observation in which a painful stimulus evokes more pain than it normally would. The group recommended standard testing for hyperalgesia by comparing the response to a single pinprick applied in the center of the most affected region to the response to an identical pinprick at the corresponding location on the unaffected limb, or an equivalent control site in the case of bilateral CRPS. The test is positive if reported pain is more intense or lasts longer on the affected limb.#

(v) *Allodynia* is a clinical observation in which pain is evoked by a stimulus that is not normally painful. Stimuli used in clinical allodynia assessment can include light touch, vibration, cool or warm temperature, deep tissue or joint pressure in the affected area, or joint movement. Only one of these is required to confirm whether allodynia is present or absent. Suggested clinical assessment procedures are now outlined as below in the revised text: "*allodynia to light touch as tested by light manual touch (or brush); allodynia to tissue pressure as assessed by pressure applied to a joint or other tissue using the evaluator's finger with just enough pressure to make the fingernail bed of the evaluator blanch (turn white)* (equating to a pressure of below 100g/cm^2, and a load of no more than 500 g; this is substantially less than the pressure recommended for the examination of tender points [4 kg/cm^2]),[6] allodynia to vibration as assessed using a graded tuning fork over bony prominence on the affected limb; allodynia to cool or warm temperature."#

(vi) Temperature asymmetry is assessed in the affected area and compared with the corresponding area on the contralateral extremity, or a suitable control site in the case of bilateral CRPS. Such asymmetry should be obvious to the touch of the dorsum of the hand of the examiner.#

(vii) Obvious color asymmetry of a regional nature (ie, hand, foot, knee, or larger region). Please specify the nature of the color changes, eg, red, blue, pale, or mottled.#

(viii) A rare limitation of the CRPS diagnostic criteria is noted: In some cases, an objective CRPS diagnostic sign such as color or temperature asymmetry may be observed by the examiner without the patient reporting the corresponding subjective symptom. This may occur, for example, because the patient cannot feel a temperature change, or a color change is difficult to see (this similarly applies to swelling). This situation may result in a patient's diagnostic symptom-category count dropping below the threshold of 3 required for formal diagnosis, despite the patient objectively displaying sufficient clinical features for diagnosis. In these instances, because of the statistical methods on which the IASP criteria were developed and validated, the obvious common-sense approach that 'signs override symptoms' (ie, a sign automatically generates a tick also as a symptom) cannot *automatically* apply. A related challenge arises also where a patient has impaired vision and is therefore unable to ascertain objective color changes; in these rare cases, a pragmatic solution must be found in which common sense prevails.

It is hoped that the modified *ICD-11* text clarifies important pragmatic aspects of CRPS assessment and diagnosis, and that it will enhance usability of these criteria in both clinical and research settings. All changes and clarifications marked with a # above have already been incorporated into the *ICD-11* CRPS text and should be applied in the CRPS diagnostic process immediately. Future research should (1) clarify whether CRPS type 1 and 2 are indeed separate entities or are better merged; (2) assess whether introduction of further subgroups such as warm-cold and early-persistent CRPS is useful (eg, for predicting treatment responses); (3) ascertain the utility of biomarkers for supporting the clinical CRPS diagnosis[1]; and (4) define "resolved CRPS."

Conflict of interest statement

The authors have no conflicts of interest to declare.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/B358.

Supplemental video content

A video abstract associated with this article can be found at http://links.lww.com/PAIN/B329.

Article history:
Received 4 January 2021
Received in revised form 19 January 2021
Accepted 22 January 2021
Available online 15 March 2021

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