**The Valencia Consensus Adaptation of the IASP CRPS Diagnostic Criteria**

The new IASP diagnostic criteria for 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 (SIG) 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.

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)

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

1. 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 three decades of CRPS experimental and clinical research clearly demonstrate 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.

1. 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 two 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 NOS (‘Not Otherwise Specified’) 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 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 (i.e., *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[[1]](#footnote-1) 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.#

1. 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):

1. 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. #
2. *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 pre-specified criteria. #
3. For evaluating possible spreading of CRPSbeyond 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. #
4. *Hyperalgesia*[[2]](#footnote-2) 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. #
5. *Allodynia*b 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)[[3]](#footnote-3), allodynia to vibration as assessed using a graded tuning fork over bony prominence on the affected limb; allodynia to cool or warm temperature.”* #
6. Temperature asymmetry is assessed in the affected area and compared to 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. #
7. Obvious color asymmetry of a regional nature (i.e. hand, foot, knee or larger region). Please specify the nature of the color changes, for example red, blue, pale, or mottled. #
8. 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’ (i.e. 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: i) clarify whether CRPS Type 1 and 2 are indeed separate entities or are better merged; ii) assess whether introduction of further subgroups such as warm-cold and early-persistent CRPS is useful (e.g., for predicting treatment responses); iii) ascertain the utility of biomarkers for supporting the clinical CRPS diagnosis[1]; iv) define ‘resolved CRPS’.

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| Table 1[[4]](#footnote-4) New IASP Diagnostic Criteria for CRPS (‘Budapest criteria’[2]) (A–D must apply) |  |
| A) The patient has continuing pain which is disproportionate to any inciting eventB) The patient reports at least one symptom in three or more of the categories C) The patient displays at least one sign in two or more of the categoriesD) 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) | 🞎 | 🞎 |

Reference List

[1] Birklein F, Ajit SK, Goebel A, Perez R, Sommer C. Complex regional pain syndrome - phenotypic characteristics and potential biomarkers. Nature reviews Neurology 2018;14(5):272-284.

[2] 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 1999/5;81(1-2):147-154.

[3] Harden RN, Bruehl S, Perez RS, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M, Ramsden C, Chont M, Vatine JJ. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. Pain 2010/8;150(2):268-274.

[4] Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology 2008/4/29;70(18):1630-1635.

[5] Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Korwisi B, Kosek E, Lavand'homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JWS, Wang SJ. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain 2019;160(1):19-27.

[6] Williams SA, Wasserman S, Rawlinson DW, Kitney RI, Smaje LH, Tooke JE. Dynamic measurement of human capillary blood pressure. Clin Sci (Lond) 1988;74(5):507-512.

1. Clinical experience and research suggest that a substantial proportion of individuals who develop CRPS resolve, with a smaller subgroup that fails to resolve even with standard care. This transition of CRPS to a more prolonged and difficult to manage condition appears 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’ of a 3-6 months pain duration in CRPS patients, 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.'  [↑](#footnote-ref-1)
2. Note that other definitions of hyperalgesia and allodynia exist for use in other chronic pain conditions ([4] Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology 2008/4/29;70(18):1630-1635.) [↑](#footnote-ref-2)
3. Equating to a pressure of below 100g/cm2,and a load of no more than 500g; this is substantially less than the pressure recommended for the examination of tender points (4kg/cm2).[6] Williams SA, Wasserman S, Rawlinson DW, Kitney RI, Smaje LH, Tooke JE. Dynamic measurement of human capillary blood pressure. Clin Sci (Lond) 1988;74(5):507-512. [↑](#footnote-ref-3)
4. Adapted from https://www.rcplondon.ac.uk/guidelines-policy/complex-regional-pain-syndrome-adults with permission [↑](#footnote-ref-4)