

Complex Regional Pain Syndrome

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CRPS

Sindrome clinica caratterizzata da:

- Dolore spontaneo ed evocato in una regione corporea SENZA distribuzione dermatomeric/territorio di un nervo periferico
- Disturbi Motori Sensitivi Autonomici Sudomotori
- Edema
- \pm anomalie trofismo
- Progressione nel tempo

Prevalenza stimata 1.2% (USA)

Lesione dei tessuti molli
e.g. distorsione/frattura
dell'arto→

*CRPS I o reflex sympathetic
dystrophy*

Lesione di un nervo
periferico→

CRPS II o causalgia



Figure 67-1. Clinical picture of a patient with complex regional pain syndrome type 1 of the upper left extremity following distortion of the left wrist.

Diagnosi precoce

- CRPS si può sviluppare ore/giorni dopo il trauma
- Il dolore si diffonde all'estremità
- Dolore profondo
- Edema dell'arto
- Aumento della temperatura vs arto controlaterale

Criteria diagnostici

Appendix II. Budapest 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

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		<input type="checkbox"/>	
B. The patient reports at least one symptom in 3 or more of the categories		<input type="checkbox"/>	
C. The patient displays at least one sign in 2 or more of the categories		<input type="checkbox"/>	
D. No other diagnosis can better explain the signs and symptoms		<input type="checkbox"/>	
Category		Symptom (the patient reports a problem)	Sign (you can see or feel a problem on examination)
1 "Sensory"	<i>Allodynia</i> (to light touch/brush stroke and/or temperature sensation and/or deep somatic pressure and/or joint movement), and/or <i>hyperalgesia</i> (to pinprick)	Reported hyperesthesia also qualifies as a symptom <input type="checkbox"/>	<input type="checkbox"/>
2 "Vasomotor"	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	<input type="checkbox"/>	<input type="checkbox"/>
3 "Sudomotor/oedema"	Oedema and/or sweating changes and/or sweating asymmetry	<input type="checkbox"/>	<input type="checkbox"/>
4 "Motor/trophic"	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)	<input type="checkbox"/>	<input type="checkbox"/>

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



Figure 1: Acute CRPS, chronic CRPS, and CRPS dystonia

(A) Acute CRPS with hyperaemia, swelling, and glossy skin. (B) Chronic, cold-type CRPS with blue discoloration of the fingers, glossy skin, and increased hair and nail growth. (C) CRPS-related dystonia of the left ankle and foot with plantar flexion and inversion of the ankle, and flexion of the toes; oedema and increased hair growth are also visible. CRPS=complex regional pain syndrome.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of Complex Regional Pain Syndrome – current state of the art. *Lancet Neurol.* 2011;10(7):637-648. doi:10.1016/S1474-4422(11)70106-5

Stadiazione

I stadio acuto

- Dolore
- Iperalgesia
- Allodinia
- Disfunzione vasomotoria/sudomotoria
- Edema +++

II stadio distrofico 3-6 mesi

- ↑ Dolore, iperalgesia, allodinia
- Disfunzione vasomotoria
- Cambiamenti trofismo/muscolo

III stadio atrofico

- ↓ Dolore, iperalgesia, allodinia
- Disfunzione vasomotoria
- Atrofia annessi e muscoli



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Stadiazione o fenotipi diversi?

Complex regional pain syndrome (CRPS) characteristics at baseline by patient subtype identified using cluster analysis.

CRPS characteristic at baseline	Warm CRPS (n = 74)	Cold CRPS (n = 78)
Self-reported symptoms (% yes)		
Allodynia or hyperalgesia	75.7	78.2
Temperature asymmetry*		
Affected side warmer	62.2	15.4
Affected side colder	0.0	76.9
Skin color asymmetry*		
Affected side red	63.5	32.1
Affected side blue/pale	10.8	37.2
Asymmetric edema*	95.9	69.2
Sweating asymmetry	56.8	51.3
Trophic changes	55.4	67.9
Motor changes†	94.6	80.8

Bruehl S, Maihöfner C,
Stanton-Hicks M, et al.
Complex regional pain
syndrome: evidence for
warm and cold
subtypes in a large
prospective clinical
sample. Pain.
2016;157(8):1674-1681.
doi:10.1097/j.pain.0000
0000000000000560

Signs observed on examination (% yes)

Allodynia	59.5	67.9
Hyperalgesia to pinprick	81.1	82.1
Temperature asymmetry*		
Affected side warmer	58.1	5.1
Affected side colder	0.0	74.4
Skin color asymmetry*		
Affected side red/mottled	62.2	34.6
Affected side blue/pale	9.5	34.6
Asymmetric edema*	87.8	53.8
Sweating asymmetry‡		
Increased on affected side	39.2	17.9
Decreased on affected side	0.0	3.8
Trophic changes§	51.4	66.7
Motor changes‡	98.6	88.5

Table 3

Presence of inflammatory complex regional pain syndrome (CRPS) characteristics at baseline and at 3-mo follow-up among patients classified into the warm and cold CRPS subtypes.

Inflammatory characteristic	Warm CRPS (n = 55)		Cold CRPS (n = 57)	
	Baseline	3-mo follow-up	Baseline	3-mo follow-up
Self-reported symptoms (% yes)				
Temperature asymmetry				
Affected side warmer	63.6	36.4	15.8	14.0
Affected side colder	0.0	16.4	75.4	54.4
Skin color asymmetry				
Affected side red	67.3	30.9	33.3	26.3
Affected side blue/pale	10.9	27.3	36.8	26.3
Asymmetric edema	94.5	65.5	66.7	64.9
Signs observed on examination (% yes)				
Temperature asymmetry				
Affected side warmer	54.5	25.5	15.8	5.3
Affected side colder	0.0	14.5	75.4	50.9
Skin color asymmetry				
Affected side red/mottled	60.0	30.9	33.3	33.3
Affected side blue/pale	10.9	12.7	36.8	28.1
Asymmetric edema	89.1	54.5	54.4	49.1

Follow-up evaluation data were only available for n = 55 of 74 and n = 57 of 78 patients classified into the warm and cold CRPS clusters, respectively, in the primary analyses. Baseline values are those observed within this select subset of patients with follow-up data.

Diagnosi differenziale

BOX 1. Possible differential diagnoses

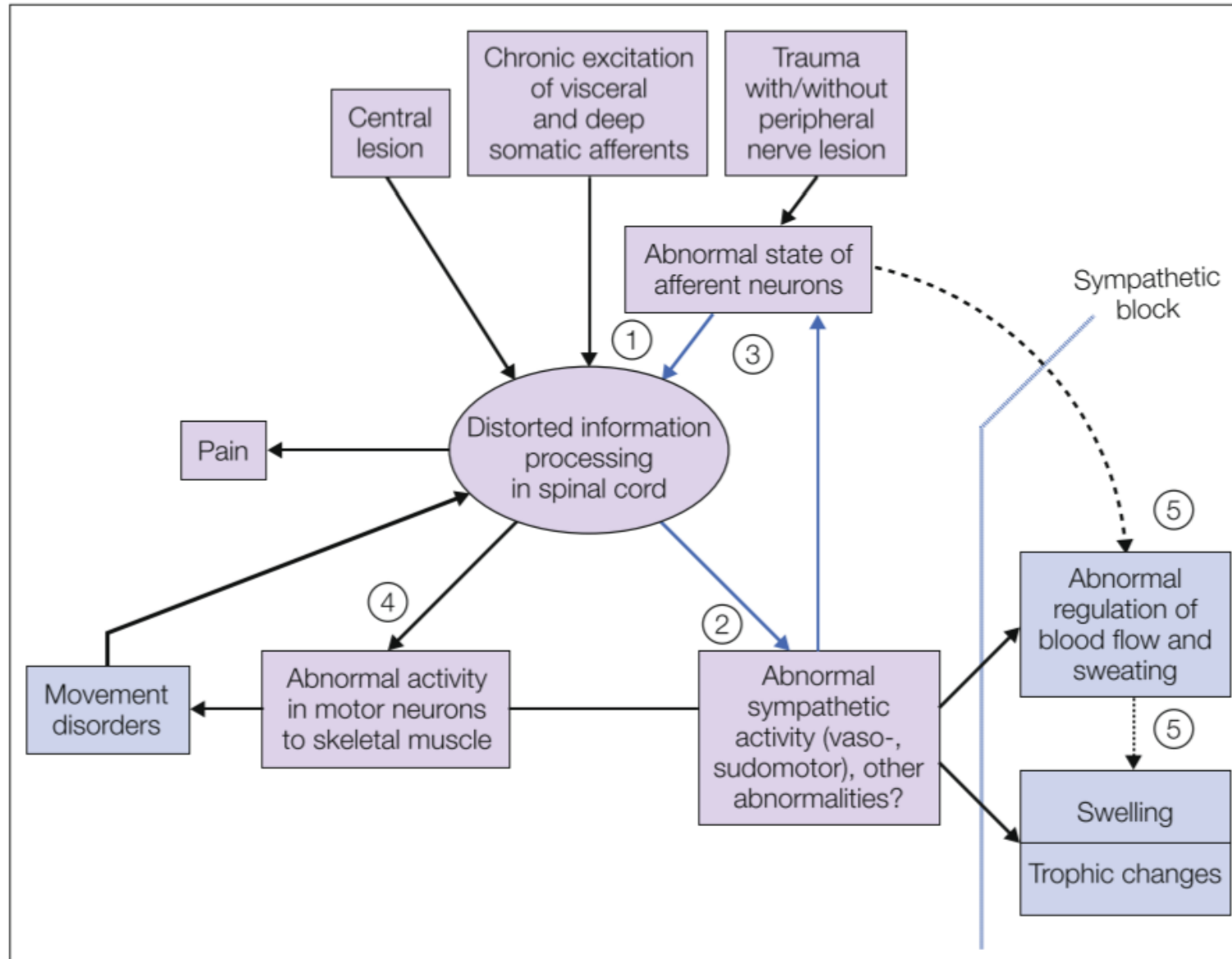
1. Local pathology: Distortion, fracture, pseudoarthrosis, arthrosis, inflammation (cellulitis, myositis, vasculitis, arthritis, osteomyelitis and fasciitis), compartment syndrome and immobilization-induced symptoms. Persistent defects after limb injury: osteoarthritis developing after joint fractures; myofascial pain due to changed (protective) movement patterns
2. Affection of arteries, veins or lymphatics, for example traumatic vasospasm, vasculitis, arterial insufficiency, thrombosis, Raynaud's syndrome, thromboangiitis obliterans (Buerger's syndrome), lymphedema and secondary erythromelalgia.
3. Connective tissue disorder
4. Central lesion, for example spinal tumour
5. Peripheral nervous system lesion (nerve compression, cervico-brachial or lumbo-sacral plexus affection, acute sensory polyneuropathy, (poly-)neuritis, autoimmune (e.g., posttraumatic vasculitis) and infectious (e.g., borreliosis))
6. Malignancy (Pancoast tumour/paraneoplastic syndrome/occult malignancy)
7. Factitious disorder

Particular awareness about differential diagnosis is advised in spontaneously developing CRPS (no trauma, about 5% of cases), when the involvement is a proximal part of the limb, such as the shoulder, or when there is primary involvement of more than one limb.



Goebel A, Barker C, Birklein F, et al. Standards for the diagnosis and management of complex regional pain syndrome: Results of a European Pain Federation task force. *Eur J Pain Lond Engl*. 2019;23(4):641-651. doi:10.1002/ejp.1362

Ipotesi fisiopatologica integrata



Terapia

3.5 Pain management—medication and procedures

“ Standard 9: Patients must have access to pharmacological treatments that are believed to be effective in CRPS. Appropriate pain medication treatments are considered broadly similar with those for neuropathic pains, although high-quality studies in CRPS are not available (Duong et al., [2018](#)). All patients with CRPS must receive a pain treatment plan consistent with any geographically relevant guidelines.

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Treatment with bisphosphonates and/or steroids has also been considered. However, the Task Force members did not reach agreement about the evidence for or against their efficacy and safety.

Goebel A, Barker C, Birklein F, et al. Standards for the diagnosis and management of complex regional pain syndrome: Results of a European Pain Federation task force. *Eur J Pain Lond Engl*. 2019;23(4):641-651. doi:10.1016/j.ejpain.2019.01.002

3.6 Physical and vocational rehabilitation

In partnership with the patient, appropriate, generally gentle, graded exercises in the presence of pain should be advised upon by a trained healthcare professional; this is essential as to give the best chance of a good outcome and minimize distress.

Immobilization of the CRPS limb should be avoided wherever possible. (Gillespie et al., 2011; Oerlemans, Oostendorp, de Boot, & Goris, 1999/10).



“ Standard 13: Patient's limb function, overall function and activity participation, including in the home and at work or school, must be assessed early and repeatedly as appropriate. Patients should have access to vocational rehabilitation (as relevant).

Standard 14: Patients with CRPS must have access to rehabilitation treatment, delivered by physiotherapists and/or occupational therapists, as early as possible in their treatment pathway.

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This may shorten the early disease course and preserve limb function. In some European countries, these treatments are guided by medical doctors, including rehabilitation specialists, general practitioners or others.

Goebel A, Barker C, Birklein F, et al. Standards for the diagnosis and management of complex regional pain syndrome: Results of a European Pain Federation task force. *Eur J Pain Lond Engl*. 2019;23(4):641-651. doi:10.1002/ejp.1362