Complex Regional Pain Syndrome

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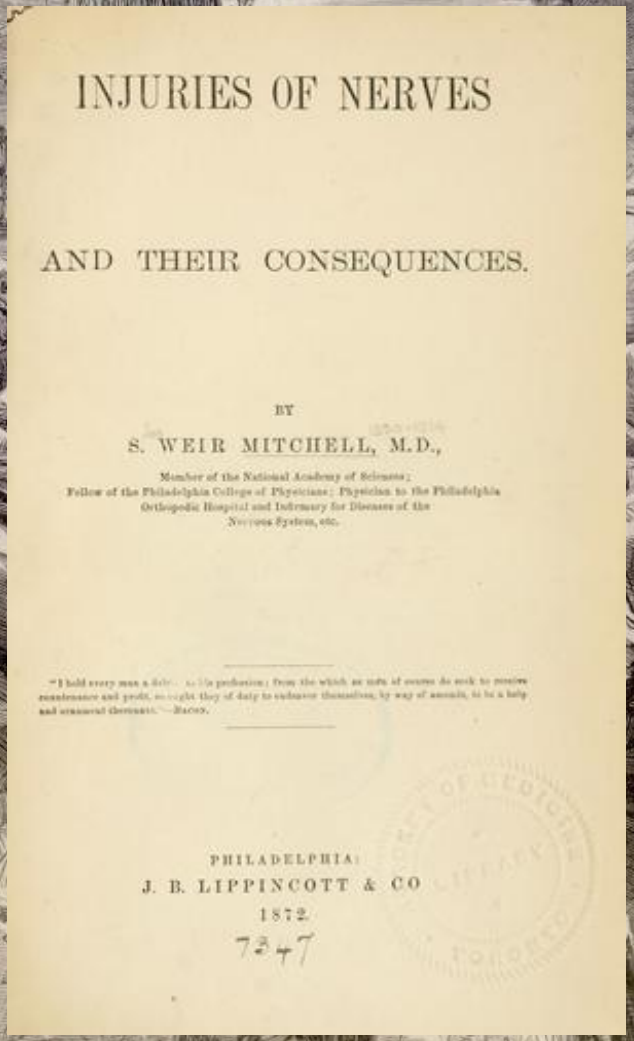
Overview

- Clinical features of CRPS
- Terminology
- Early recognition
- Who to refer to ?
- Acknowledge important role APS/physio play

Causalgia



INJURIES OF NERVES

AND THEIR CONSEQUENCES.

BY

S. WEIR MITCHELL, M.D.,

Member of the National Academy of Sciences;
Fellow of the Philadelphia College of Physicians; Physician to the Philadelphia Orthopedic Hospital and Infirmary for Diseases of the Nervous System, etc.

"I hold every man a debtor to his profession; from the which as men of course do seek to receive countenance and profit, so ought they of duty to endeavor themselves, by way of amends, to be a help and ornament thereunto."—BACON.

PHILADELPHIA:
J. B. LIPPINCOTT & CO
1872

7247

‘Perhaps few persons who are not physicians can realise the influence which long continued and unendurable pain may have upon both body and mind …Under such torments the temper changes, the most amiable grow irritable, the soldier becomes a coward, and the strongest man is scarcely less nervous than the most hysterical girl.’

S.Weir Mitchell, 1872

History

Leriche

sympathetic nervous system dysfunction implicated as mechanism

surgical sympathectomy

Disease formerly known as….

- CRPS I = Reflex Sympathetic Dystrophy
- CRPS II = Causalgia

Algodystrophy,

Sudeck’s atrophy,

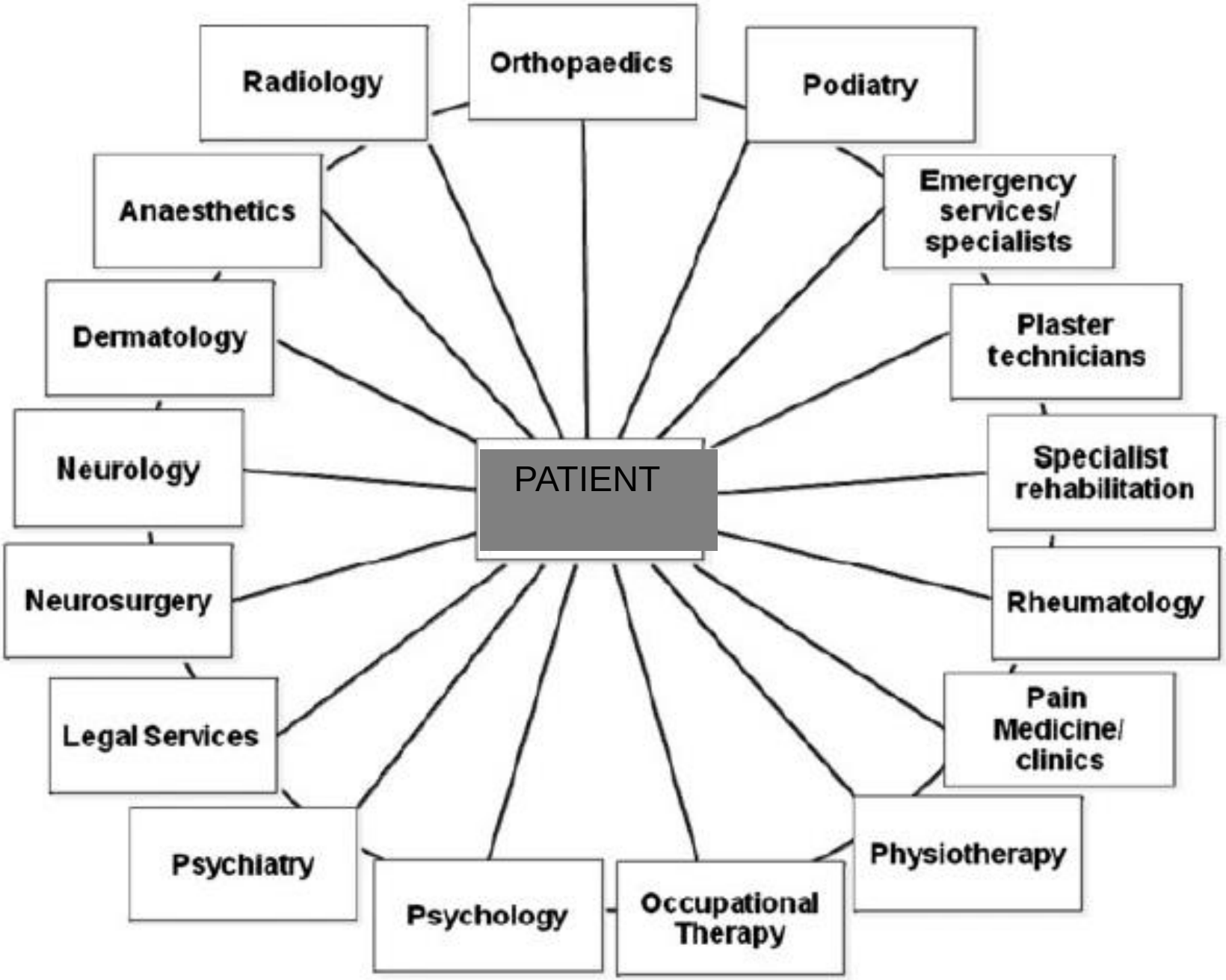
Sympathetically maintained pain,

Shoulder/hand syndrome.

CRPS

- Complex: Varied and dynamic clinical presentation
- Regional: Non-dermatomal distribution of symptoms
- Pain: Out of proportion to the inciting events
- Syndrome: Constellation of symptoms and signs

Variable progression over time


Radiology
Orthopaedics
Podiatry
Anaesthetics
Emergency services/ specialists
Dermatology
Plaster technicians
Neurology
PATIENT
Specialist rehabilitation
Neurosurgery
Rheumatology
Legal Services
Pain Medicine/ clinics
Psychiatry
Physiotherapy
Psychology
Occupational Therapy

What is CRPS ?

Severe Pain

Hypersensitivity

Swelling

Discoloration

Temperature Change

Abnormal sweating

Dystonia

Disability/Distress

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.

Table 1. Distinct Factors of CRPS	
Symptoms	**Comments**
Continuing regional pain	• Disproportionate to any inciting event
Sensory	• Hyperesthesia • Allodynia
Vasomotor	• Temperature asymmetry • Skin color changes • Skin color asymmetry
Sudomotor/Edema	• Swelling due to fluid in the body's tissues • Sweating changes • Sweating asymmetry
Motor/Trophic	• Decreased range of motion • Motor dysfunction • Changes in hair, skin, and nails

CRPS, complex regional pain syndrome
Based on reference 4 and Harden RN, et al. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Med.* 2007;8(4):326-331.

Table 2. Differential diagnosis of complex regional pain syndrome.[4]

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Neuropathic pain syndromes
• Peripheral (poly) neuropathy
• Nerve entrapment
• Radiculopathy
• Post-herpetic neuralgia
• De-afferentation pain post-cerebrovascular accident
• Plexopathy
• Motor neuron disease
Vascular diseases
• Thrombosis
• Acrocyanosis
• Atherosclerosis
• Raynaud's phenomenon
• Erythromelalgia
Inflammation
• Erysipelas
• Inflammation-not otherwise specified
• Bursitis
• Seronegative arthritis
• Rheumatologic diseases
Myofascial pain syndromes
• Overuse
• Disuse
• Tennis elbow
• Repetitive strain injury
• Fibromyalgia
Psychiatric problems
• Somatoform pain disorders
• Munchhausen syndrome

Aetiology of CRPS

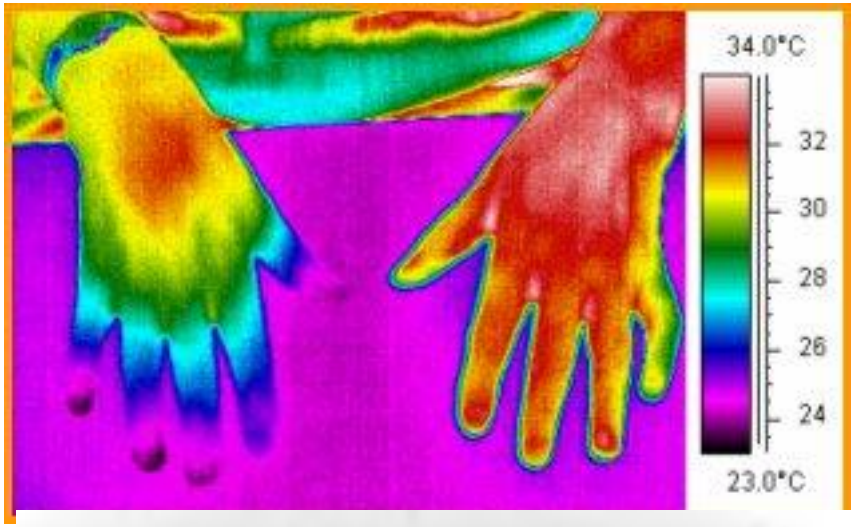
Cause	Incidence
Fracture[1,2,4]	16%
Strain or sprain[1,2]	10–29%
Post surgery[1,2,3,4]	3–24%
Contusion or crush injury[1,2]	8%
Spontaneous[2]	6%
Other causes or unknown etiology[1,2]	2–17%

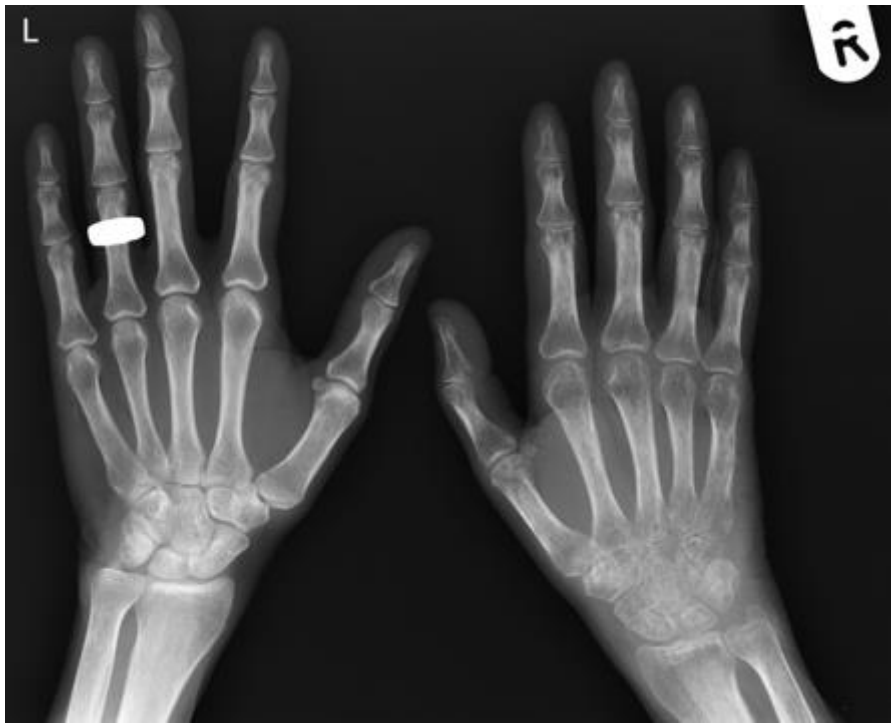
1. Harden RN et al. Pain 1999;83:211-219
2. Allen G et al. Pain 1999;80:539-44
3. Cobb TK, Morrey B. J Bone Joint Surg Am 1997;79:826-32
4. Prosser R, Conolly WB. J Hand Ther 1996; 9(4):344-8

Epidemiology

- Incidence: 5.46/100,000/year
- Prevalance: 20.57/100,000
- Female:Male ratio: 3-4:1
- Peak incidence 61-70yrs

Investigations

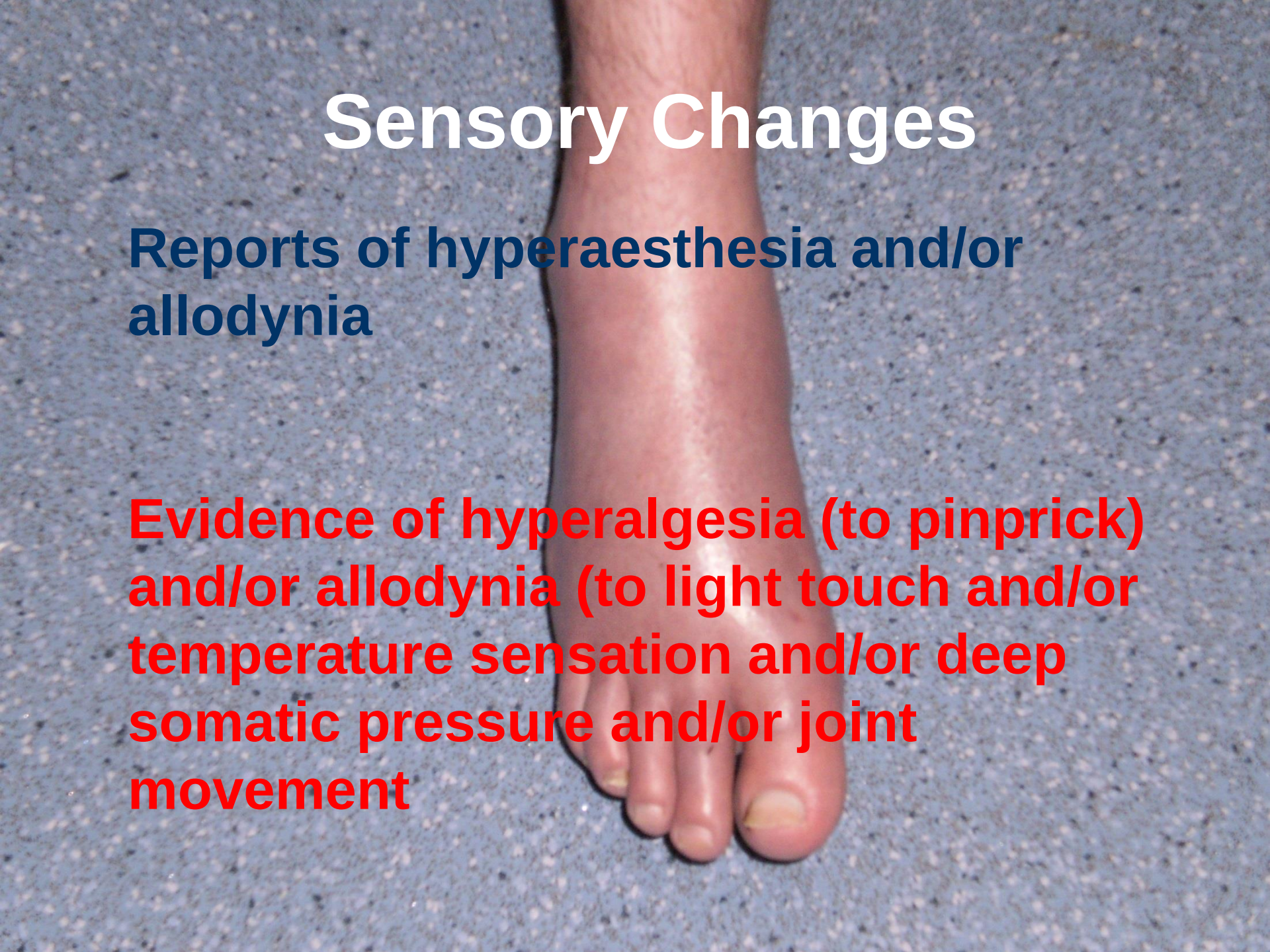




Proposed clinical diagnostic criteria for CRPS

Continuing pain disproportionate to the inciting event

There is no other diagnosis that better explains the symptoms and signs

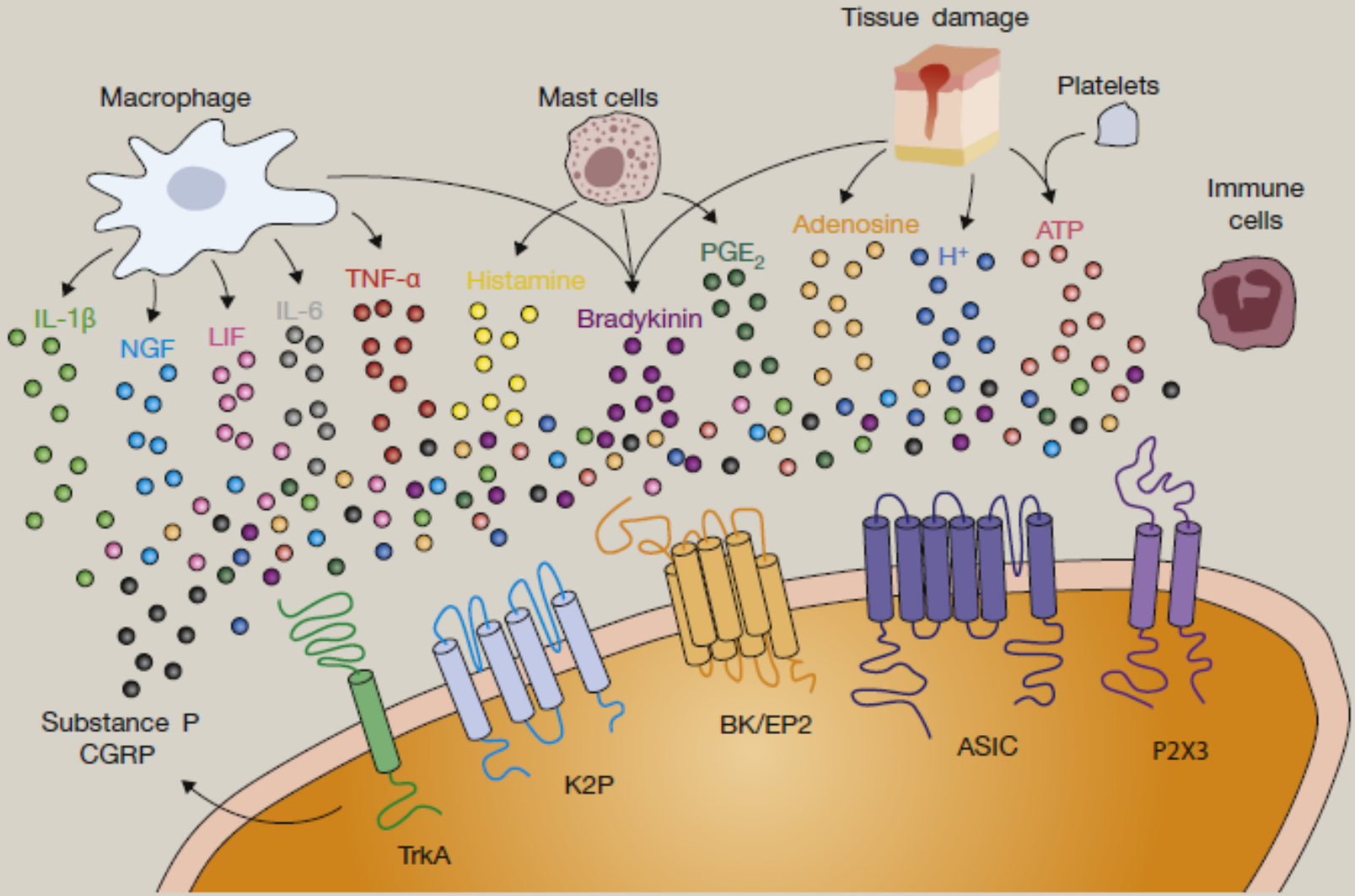


Sensory Changes

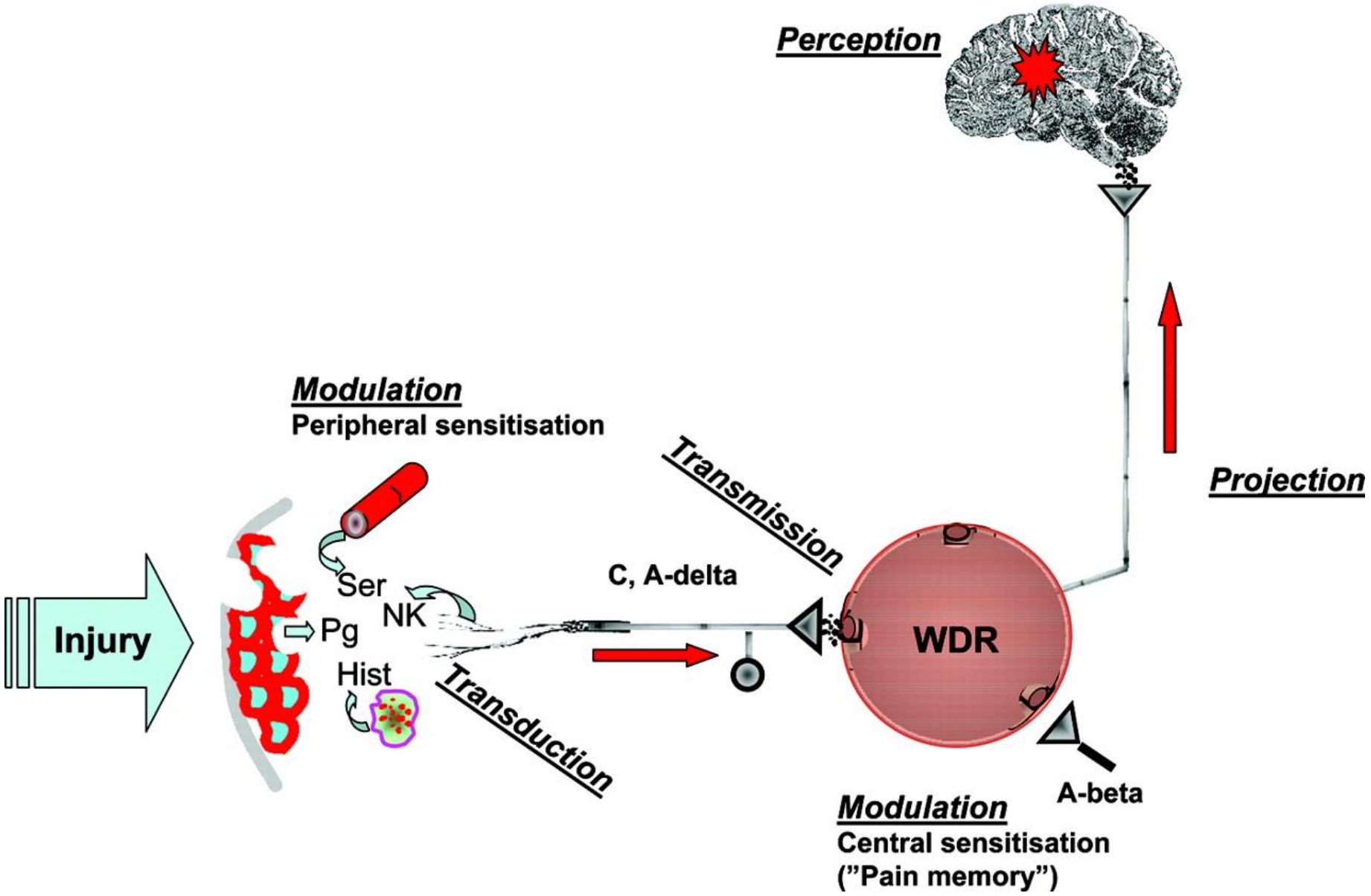
Reports of hyperaesthesia and/or allodynia

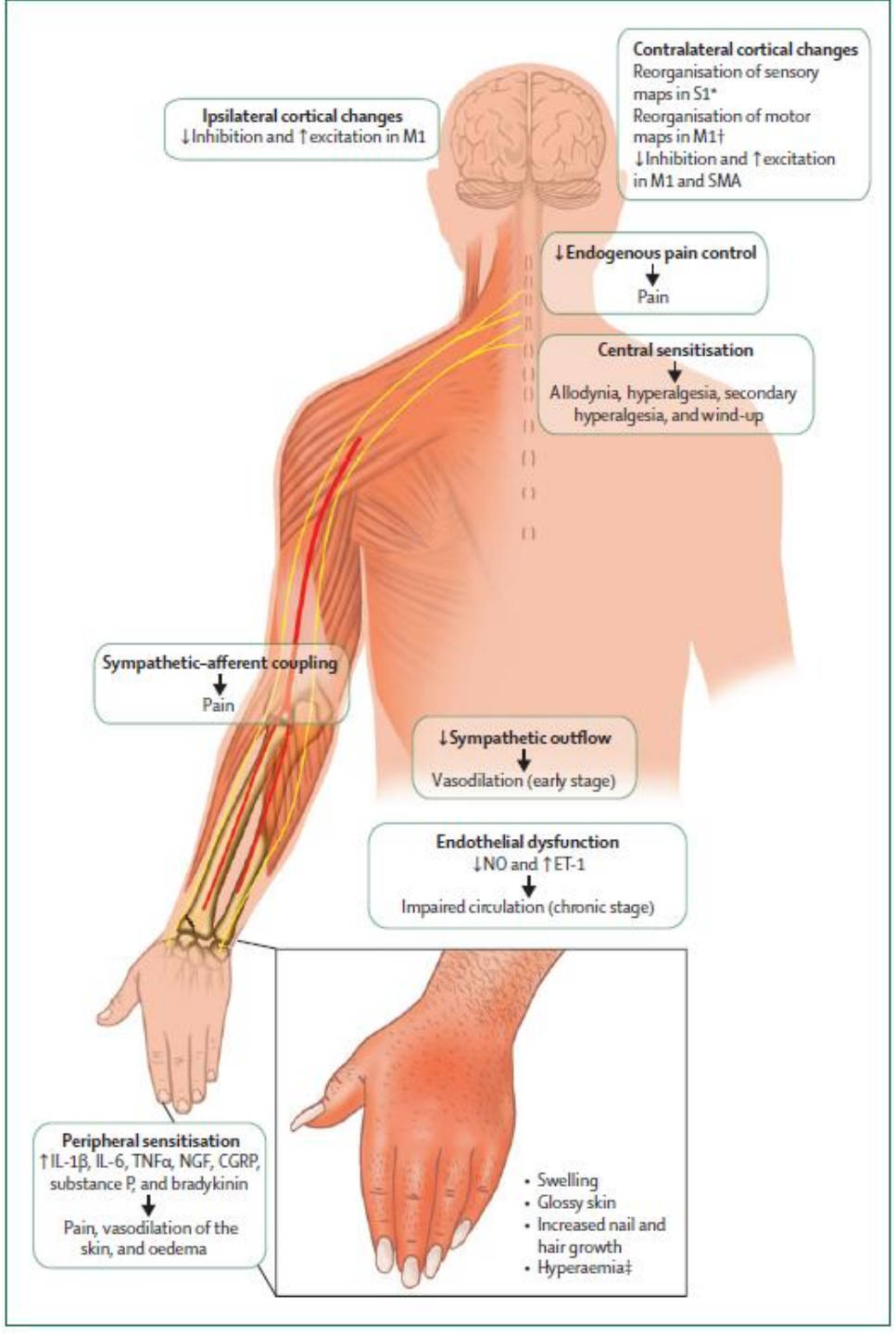
Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement

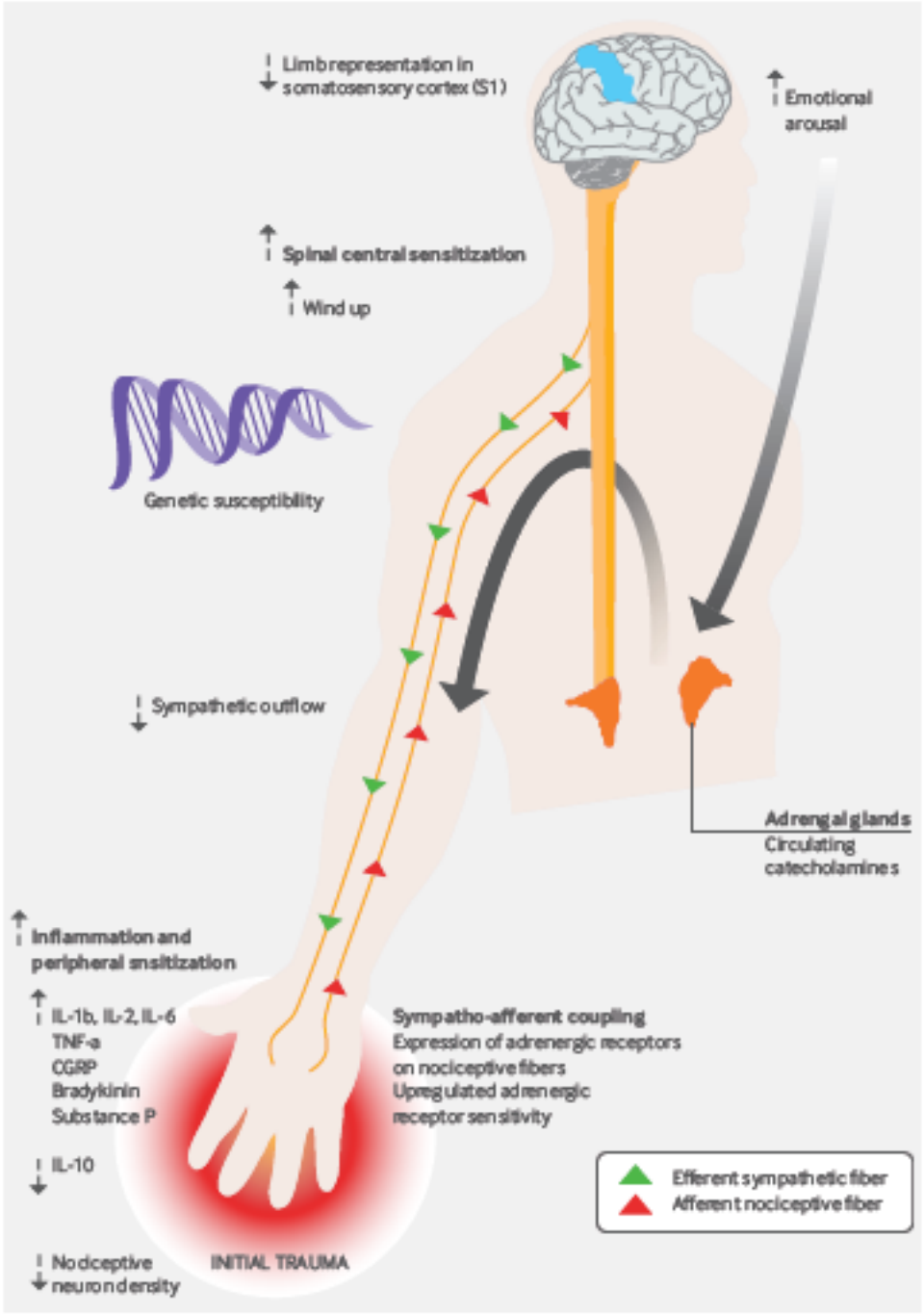
Mechanisms of peripheral sensitization

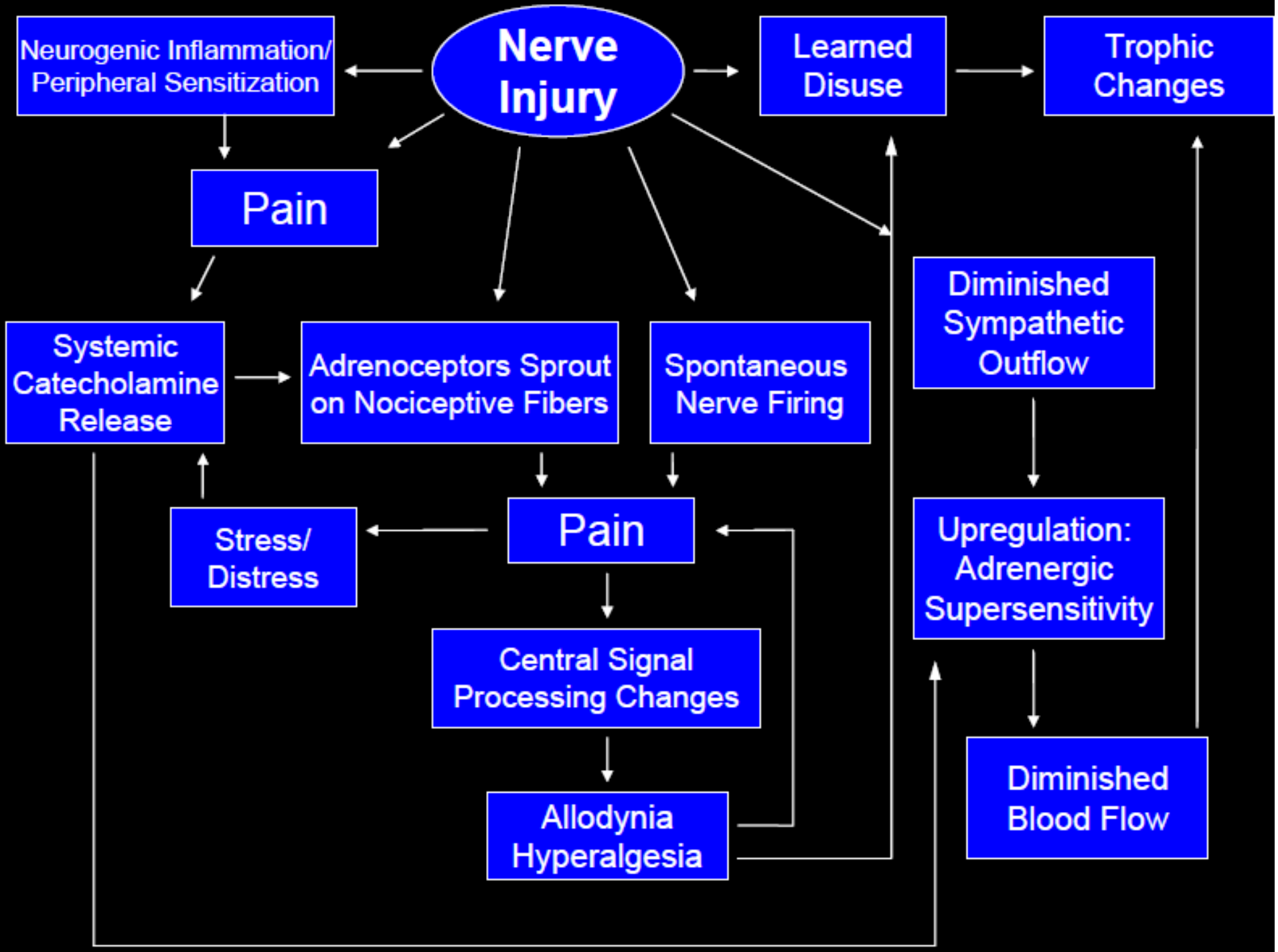


Modified from Basbaum AI *et al. Cellular and Molecular Mechanisms of Pain.* Cell 2009; **139**: 267–81.
ASIC, acid-sensing ion-channel; BK, bradykinin receptor; EP2, EP2 prostaglandin receptor; H^+, proton; IL-1β, interleukin-1β; IL-6, interleukin-6; K2P, two-pore potassium channel; NGF, nerve growth factor; P2X3, ATP receptor; PGE_2, prostaglandin E_2; TNF-α, tumour necrosis factor-α; TrkA, high affinity NGF receptor


Perception
Modulation
Peripheral sensitisation
Transmission
Projection
Ser
NK
Pg
Hist
C, A-delta
Injury
WDR
Transduction
A-beta
Modulation
Central sensitisation
("Pain memory")


Contralateral cortical changes
Reorganisation of sensory maps in S1*
Reorganisation of motor maps in M1†
↓Inhibition and ↑excitation in M1 and SMA
Ipsilateral cortical changes
↓Inhibition and ↑excitation in M1
↓Endogenous pain control
Pain
Central sensitisation
Allodynia, hyperalgesia, secondary hyperalgesia, and wind-up
Sympathetic–afferent coupling
Pain
↓Sympathetic outflow
Vasodilation (early stage)
Endothelial dysfunction
↓NO and ↑ET-1
Impaired circulation (chronic stage)
Peripheral sensitisation
↑IL-1β, IL-6, TNFα, NGF, CGRP, substance P, and bradykinin
Pain, vasodilation of the skin, and oedema
• Swelling
• Glossy skin
• Increased nail and hair growth
• Hyperaemia‡


Limb representation in somatosensory cortex (S1)
Emotional arousal
Spinal central sensitization
Wind up
Genetic susceptibility
Sympathetic outflow
Adrengal glands
Circulating catecholamines
Inflammation and peripheral sensitization
IL-1b, IL-2, IL-6
TNF-a
CGRP
Bradykinin
Substance P
IL-10
Nociceptive neurondensity
INITIAL TRAUMA
Sympatho-afferent coupling
Expression of adrenergic receptors on nociceptive fibers
Upregulated adrenergic receptor sensitivity
Efferent sympathetic fiber
Afferent nociceptive fiber


Nerve Injury
Neurogenic Inflammation/ Peripheral Sensitization
Learned Disuse
Trophic Changes
Pain
Systemic Catecholamine Release
Adrenoceptors Sprout on Nociceptive Fibers
Spontaneous Nerve Firing
Diminished Sympathetic Outflow
Stress/ Distress
Pain
Upregulation: Adrenergic Supersensitivity
Central Signal Processing Changes
Allodynia Hyperalgesia
Diminished Blood Flow

Mechanisms

Box 2 | Possible mechanisms involved in complex regional pain syndrome

Nerve injury[31-34]

Ischemic reperfusion injury or oxidative stress[35-40]

Central sensitization[41-43]

Peripheral sensitization[44 45]

Altered sympathetic nervous system function or sympatho-afferent coupling[46-52]

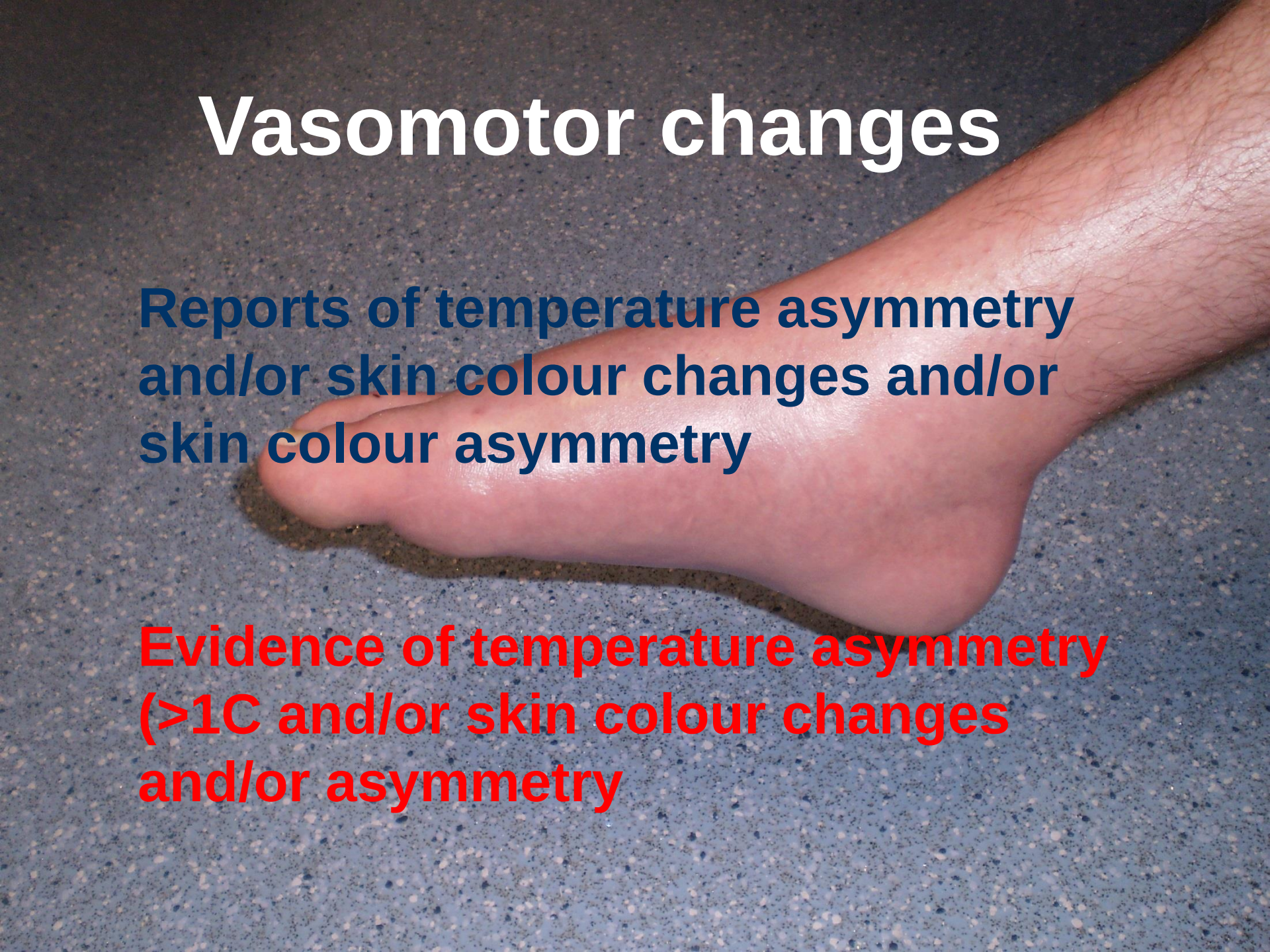
Inflammatory and immune related factors[53-77]

Brain changes[78-89]

Genetic factors[90-92]

Psychological factors and disuse[93-103]

Vasomotor changes



Reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry

Evidence of temperature asymmetry (>1C and/or skin colour changes and/or asymmetry

Sudomotor Changes and oedema

Reports of oedema and/or sweating changes and/or sweating asymmetry

Evidence of oedema and/or sweating changes and/or sweating asymmetry

Motor/Trophic changes

Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair,nail,skin)

Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair,nail,skin)

Complex regional pain syndrome diagnostic criteria

2003 Budapest revised criteria

All criteria required for diagnosis

CRITERION 1
Pain disproportionate to inciting event

CRITERION 2
At least one SYMPTOM from each of three distinct categories below

CRITERION 3
At least one SIGN from each of two distinct categories below

CRITERION 4
No other diagnosis that might account for signs and symptoms

CATEGORIES

- SENSORY: Allodynia, hyperalgesia
- VASOMOTOR: Temperature asymmetry, skin colour change or asymmetry
- SUDOMOTOR: Oedema, sweating change or asymmetry
- MOTOR/TROPHIC: Decreased range of movement, weakness, dystonia, tremor, skin/hair/nail changes

Early CRPS
0 – 3 months

Severe Pain Disproportionate

Limited movement

Swelling

Red/warm

? Mild forms common in Fracture/Ortho clinics

5 Cardinal signs of inflammation

Pain

Oedema

Erythema

↑ Temperature

Loss of function

Medium term (Dystrophic) 6 weeks - 1year

Persistent Pain Hypersensitivity

Swelling spreads

Limb colder

Hair/nail changes

Abnormal sweating

Soft tissue/muscle wasting

Neglect

Late (Atrophic) >1 year

Persistent pain

‘Cold’ blue/mottling

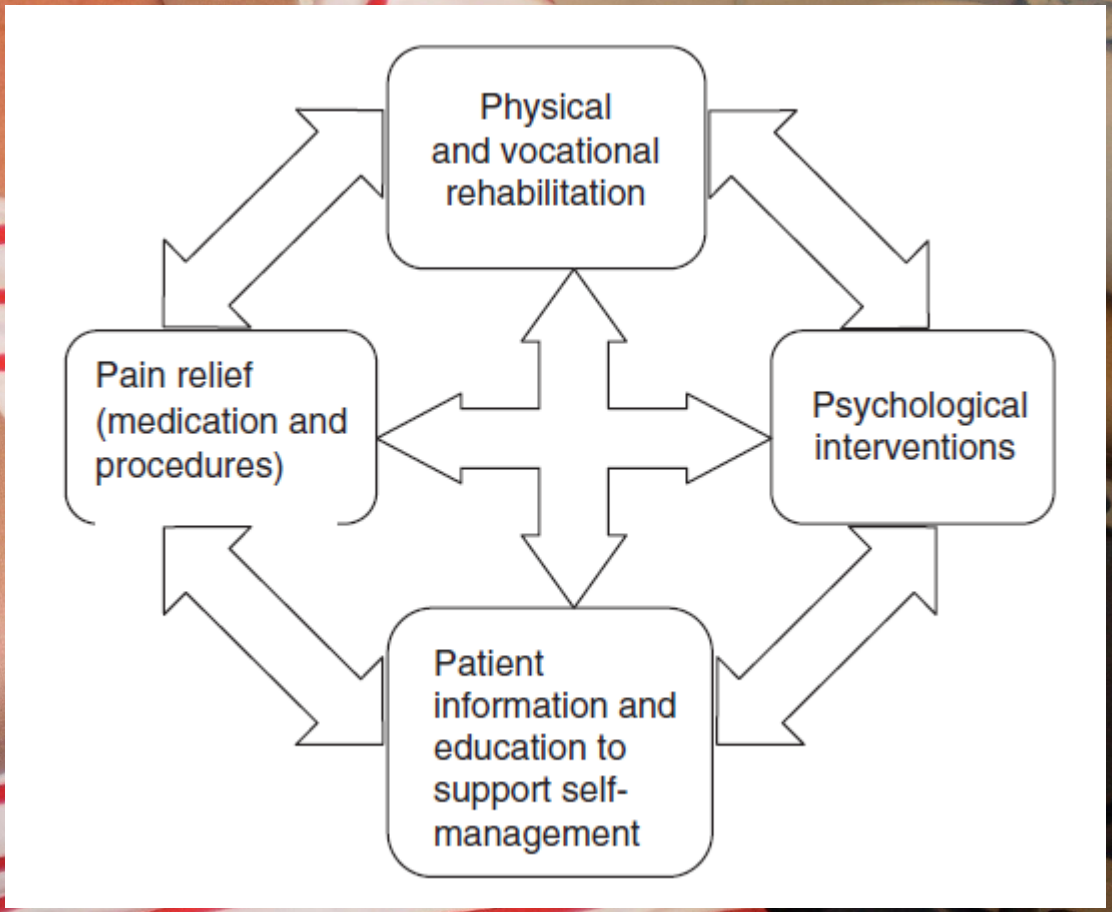
Peri-articular thickening

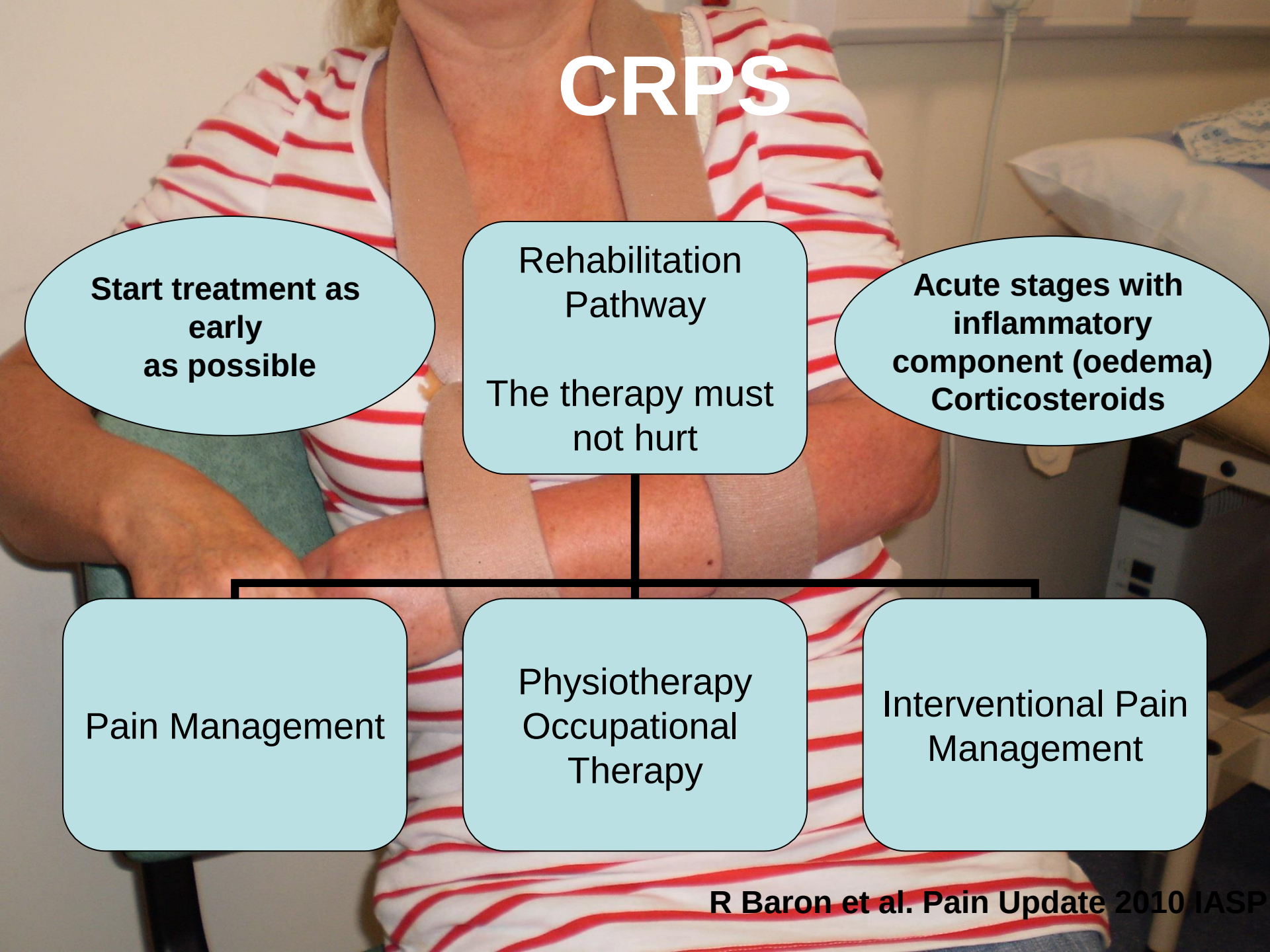
Stiff joints

Muscle atrophy

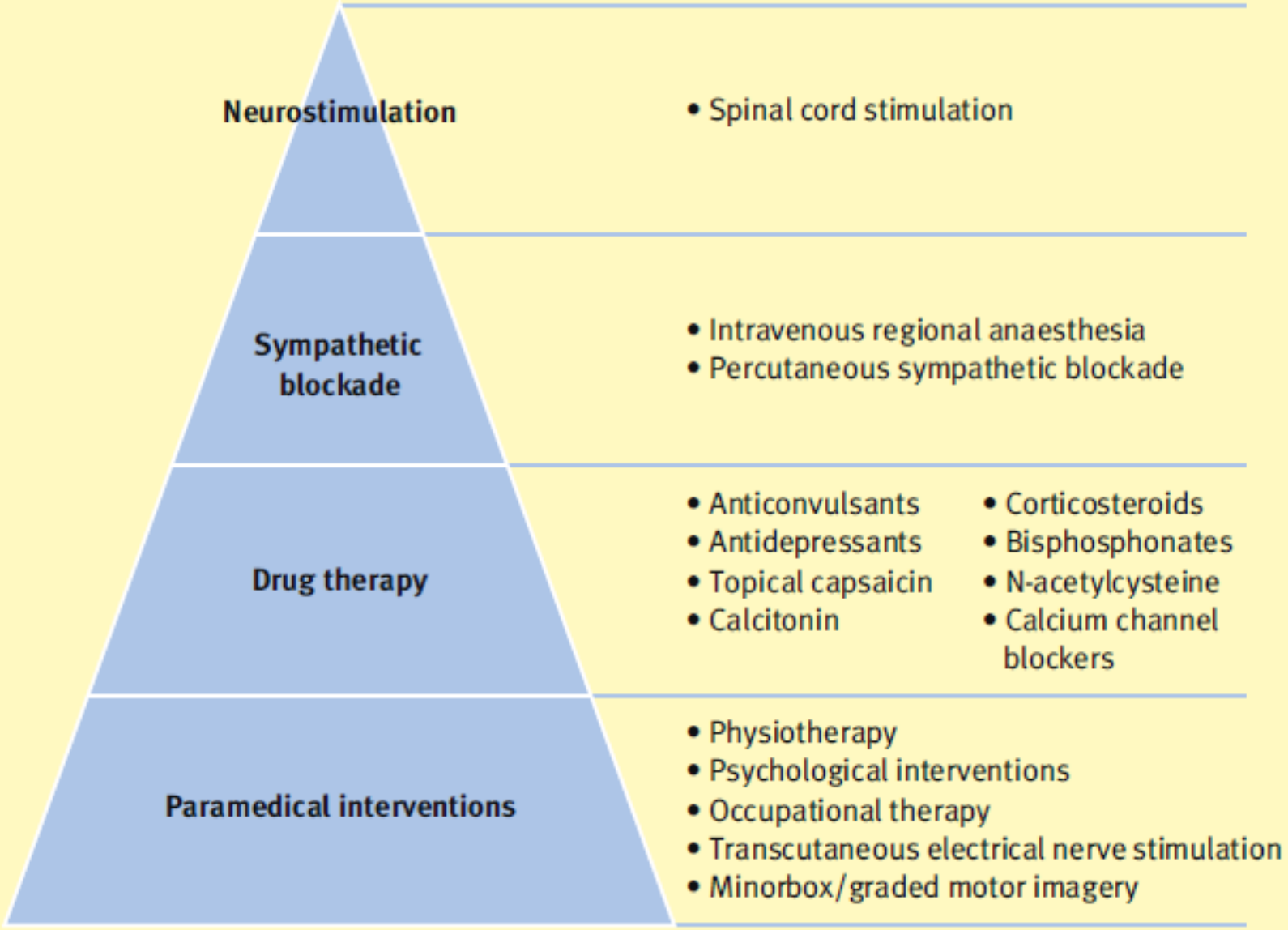
Spasms/dystonia/tremor

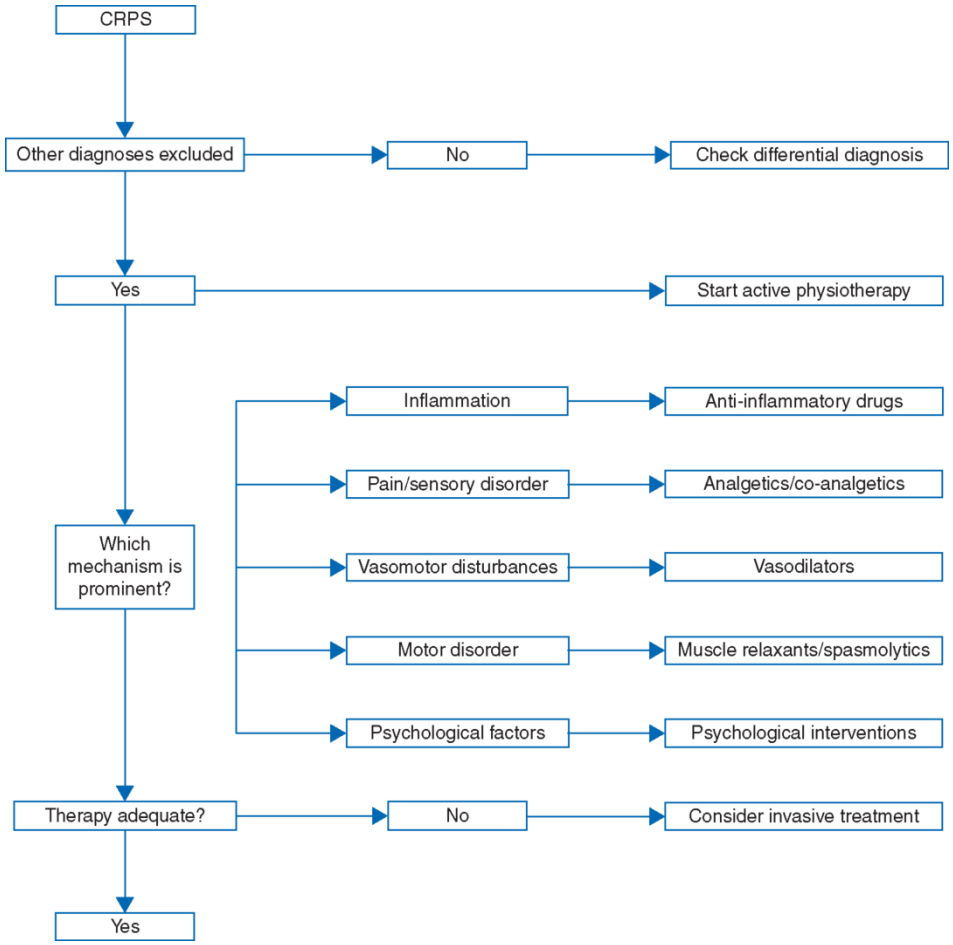
CRPS


Physical and vocational rehabilitation
Pain relief (medication and procedures)
Psychological interventions
Patient information and education to support self-management


CRPS
Start treatment as early as possible
Rehabilitation Pathway
The therapy must not hurt
Acute stages with inflammatory component (oedema) Corticosteroids
Pain Management
Physiotherapy Occupational Therapy
Interventional Pain Management
R Baron et al. Pain Update 2010 IASP

Treatment options





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Summary of treatments for complex regional pain syndrome (CRPS)

Treatment	Category	Supporting RCT status
Multidisciplinary treatment	Standard	None
Physical and occupational therapy	Standard	Positive[150 153]
Oral corticosteroids (for acute CRPS)	Standard	Positive[150 162]
Anticonvulsants	Standard	Equivocal[164]
Analgesic antidepressants	Standard	None
Transdermal lidocaine	Standard	None
Opioids	Standard	None
Sympathetic nervous system blocks	Standard	Negative[150 153]
Spinal cord stimulation	Standard	Positive (<5 year efficacy)[167 168]
Pain focused psychological therapy	Standard	None
Graded motor imagery or mirror therapy	Uncommon	Positive[153 158]
Calcitonin	Uncommon	Positive[153]
Vitamin C (prevention after injury)	Uncommon	Positive[150 171-174 176]
Topical dimethylsulfoxide (DMSO)	Uncommon	Positive (warm CRPS)[150]
Oral N-acetylcysteine	Uncommon	Positive (cold CRPS)[150]
Bisphosphonates	Emerging	Positive[150 153 181-184]
Subanesthetic intravenous ketamine	Emerging	Positive[150 153 186 187]
Intravenous immunoglobulin	Emerging	Positive[189]
Oral tadalafil	Emerging	Positive[190]
Intrathecal baclofen (CRPS + dystonia)	Emerging	Positive[191]
Low dose oral naltrexone	Emerging	None

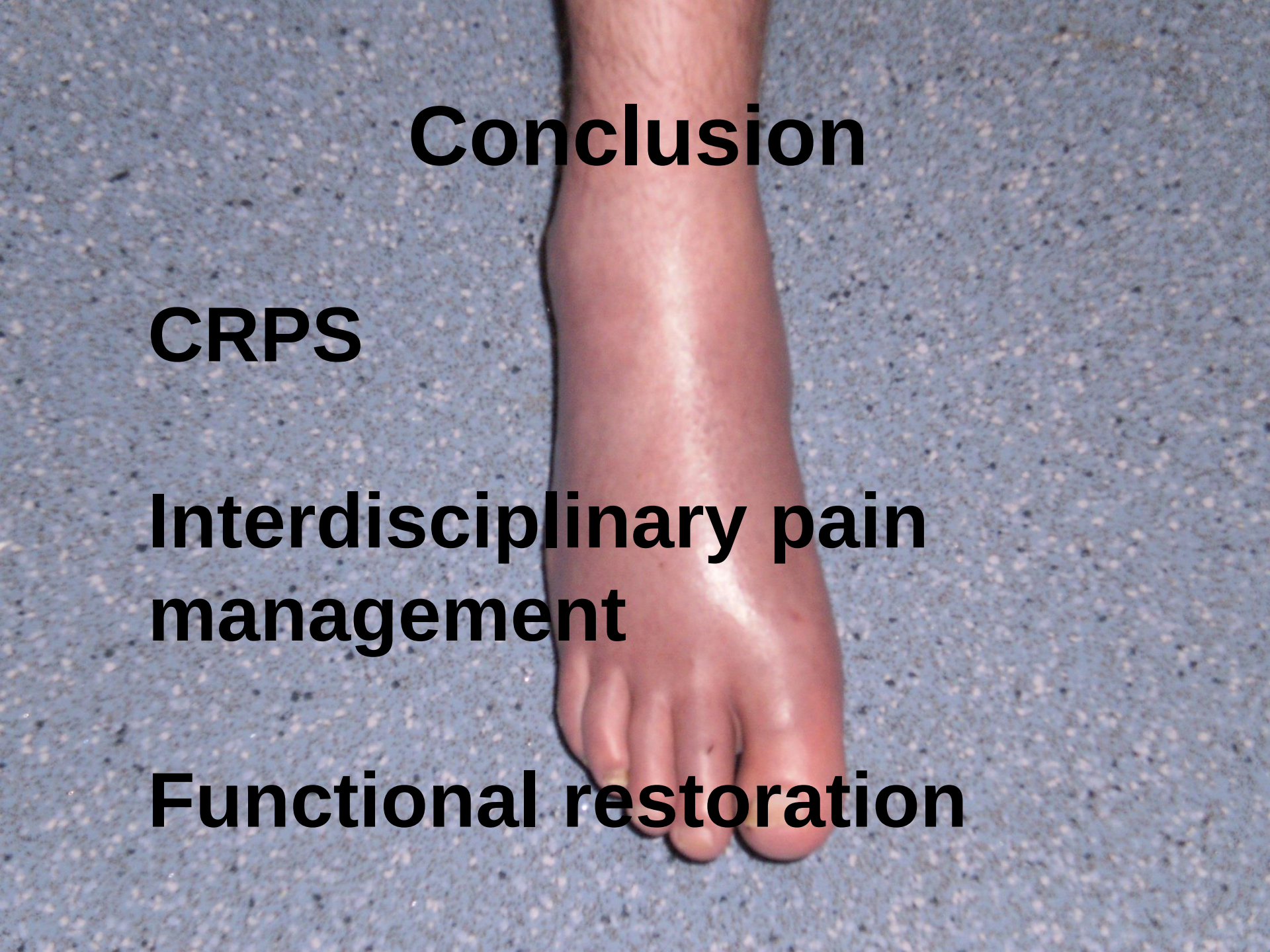
RCT=randomized controlled trial.

Outcome

- 30% Recover
- 55% Stable
- 15% syndrome persists >6yrs after onset

Key Points

- Complex regional pain syndrome (CRPS) is a disabling condition that needs timely recognition by the clinician for effective therapy.
- The Budapest criteria have more specificity than the International Association for the Study of Pain criteria.
- There are multiple theories on the pathogenesis of CRPS—it probably is a result of multimodal pathogenesis.
- CRPS diagnosis is essentially clinical although some investigations may be useful.
- The four pillars of treatment of CRPS are patient education, physical rehabilitation, pain management, and psychological interventions.


Conclusion
CRPS
Interdisciplinary pain management
Functional restoration

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safe • clean • personal

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