Tassonomia “a tavolino” e clinica “nel mondo reale”: il puzzle del dolore cronico

I CONGRESSO NAZIONALE SOCIETÀ ITALIANA G.U.I.D.A.
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Don't forget

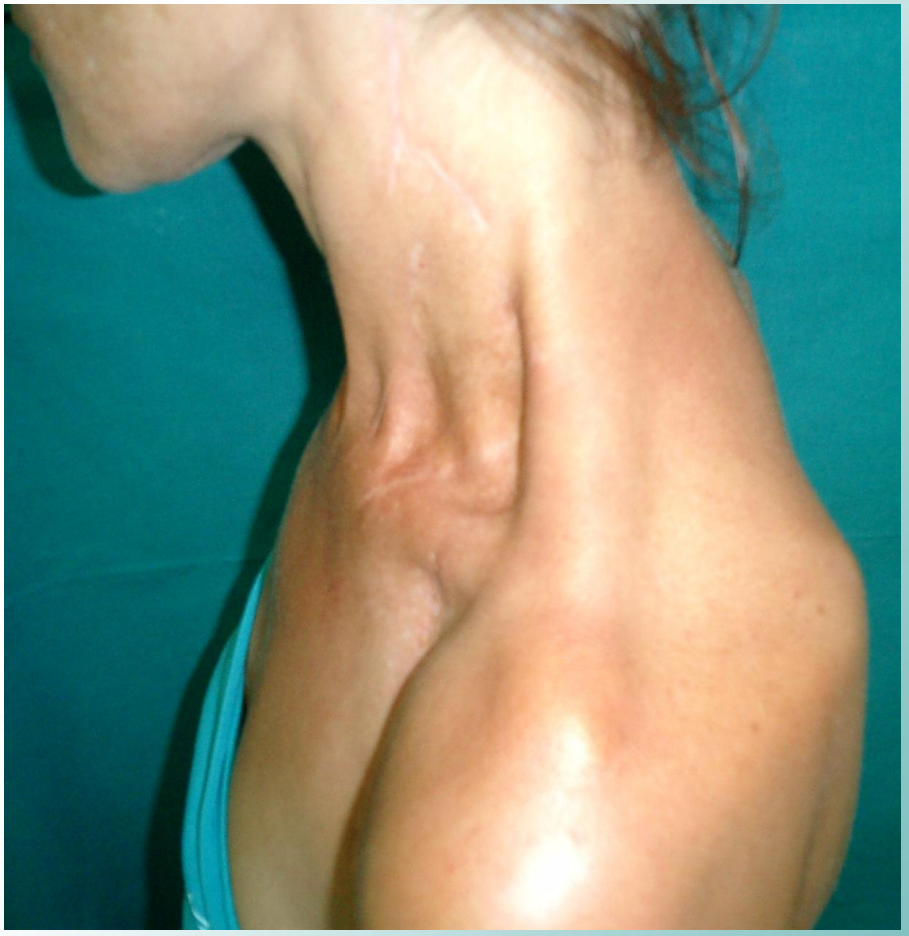
- Pain is too often referred as being a simple homogeneous experience (pain is pain)
- A statement basically wrong as the term *pain* encompasses several and different subjective experiences
- My pain is not your pain
- Today's pain is not yesterday's pain

EFIC School, 2009

Don’t forget

- These experiences are linked only by what Wittgenstein calls “**familial resemblances**” rather than to a common core
- Pain is an abstraction and in the day life it is reported under physical, emotional multiple and distinct clinical picture

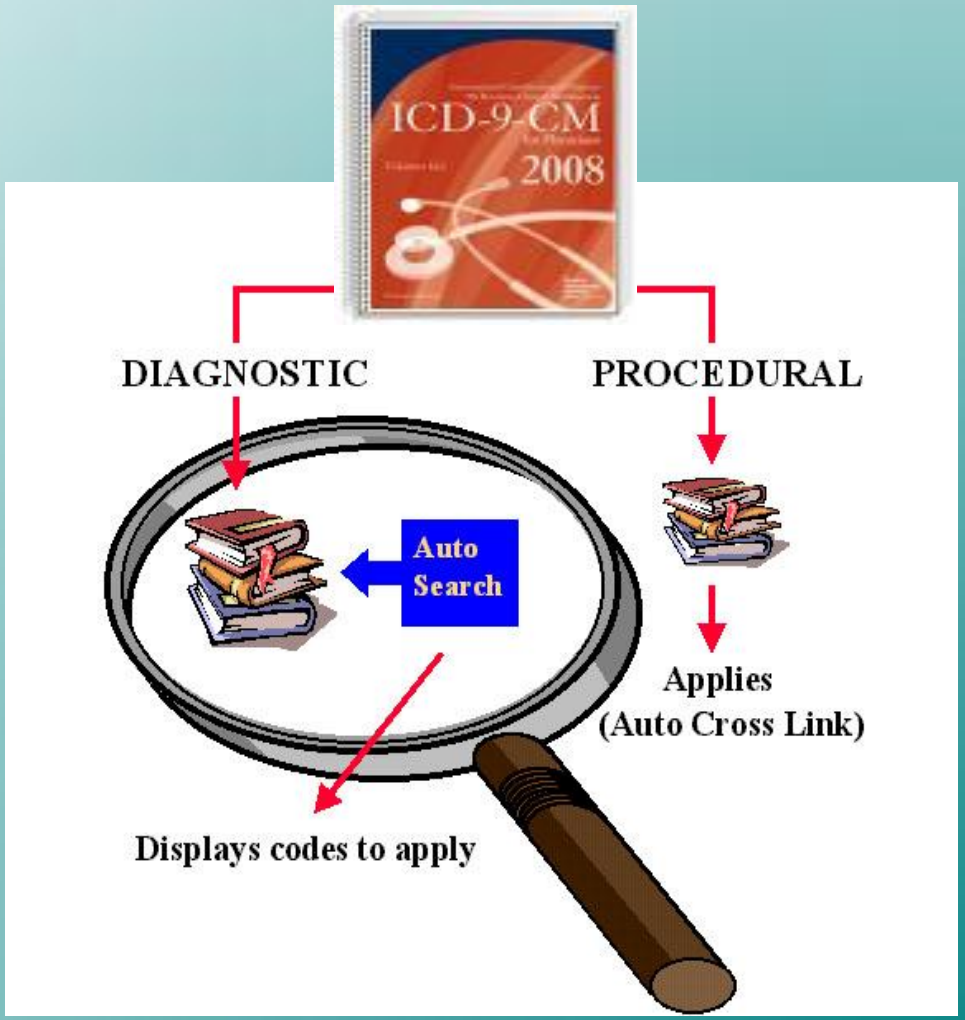
We have other limits…



- Neurological and psychological mechanisms of chronic pain are complex and still not completely clear
- Controversies are present even in the classification of pain states and drugs
- The clinical setting greatly influences pain assessment (age, language and environment, cognitive status, gender…and
- doctors)
- Vulnerable subjects (minimally responsive subjects, poor cultural level, old people etc) pose assessment problems

The Medical and social system have limits

- Pain clinical assessment guidelines (if present) are always considered **only during the first interview.**
- Correct diagnostic codes are lacking (International Classification of Diseases, 9° revision - ICD-9-CM)
- **ICF classification (CWP)**
- Reimbursements are not satisfactory



Other uncomfortable hints

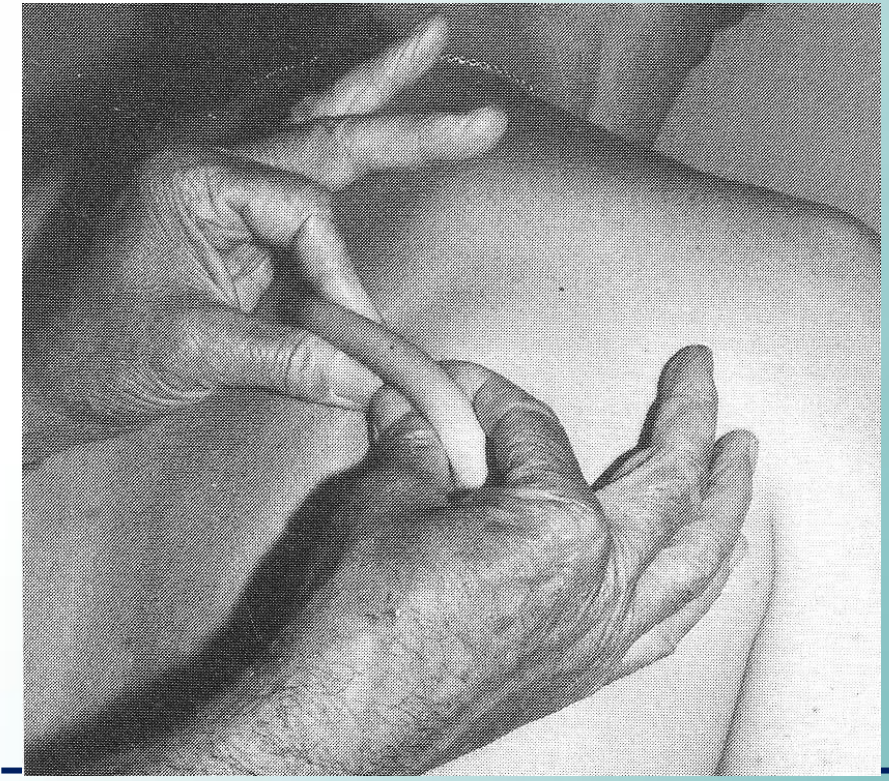
- The same disease can show different pain symptoms and patterns
- The same patient may have several kinds of abnormal pain sensations
- One kind of abnormal sensation may be generated by different underlying mechanisms.
- Different diseases can have similar symptoms
- A single disease can be associated with more than one type of pain

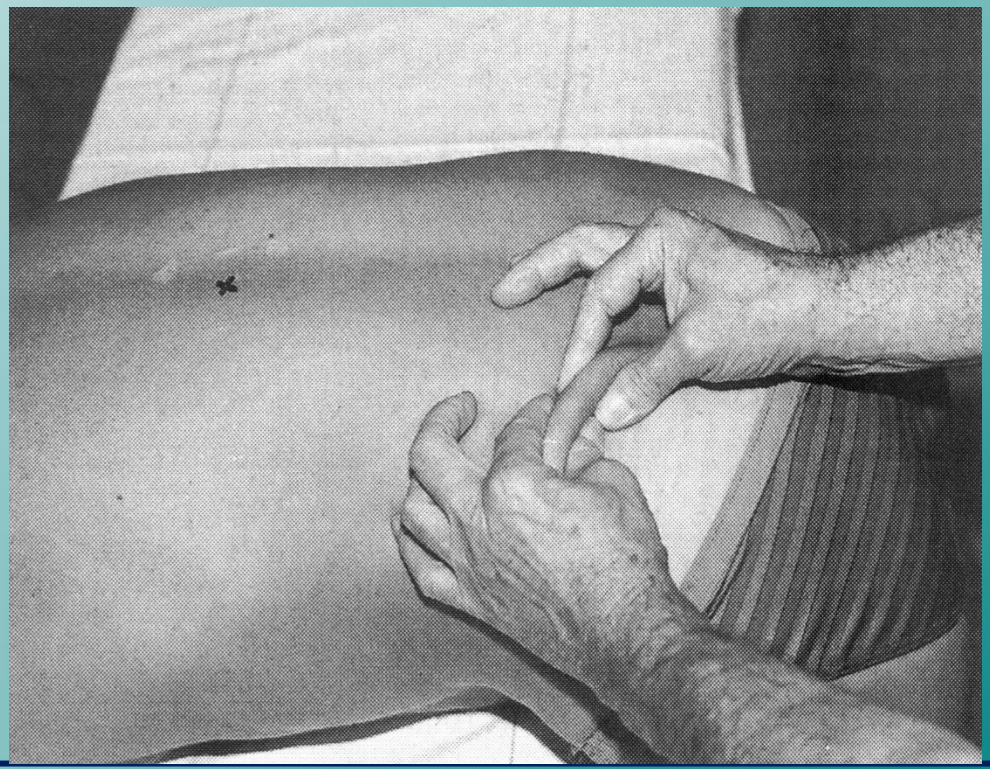
The NEW ENGLAND JOURNAL of MEDICINE

Muscle pain and fatigue affect nearly half of patients who seek medical care. One of the paradoxes of medicine is that patients with these symptoms seldom have a recognizable disorder of muscle that can be identified by objective diagnostic tests such as muscle biopsy, electrophysiology, or imaging. The inability to arrive at a specific diagnosis is frustrating to both patients and physicians.

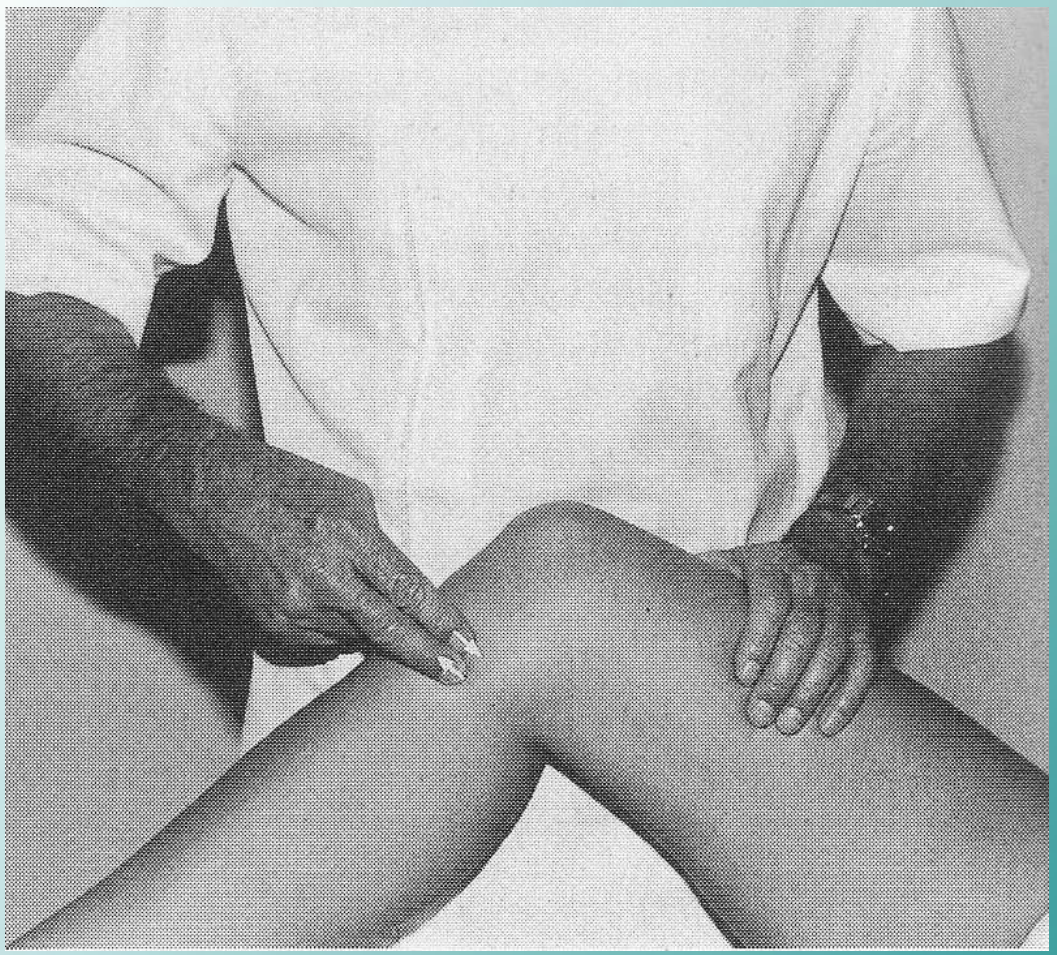
Editoriale, Volume 341:1076-1078,14, 1999.

The skin is not a muscle…

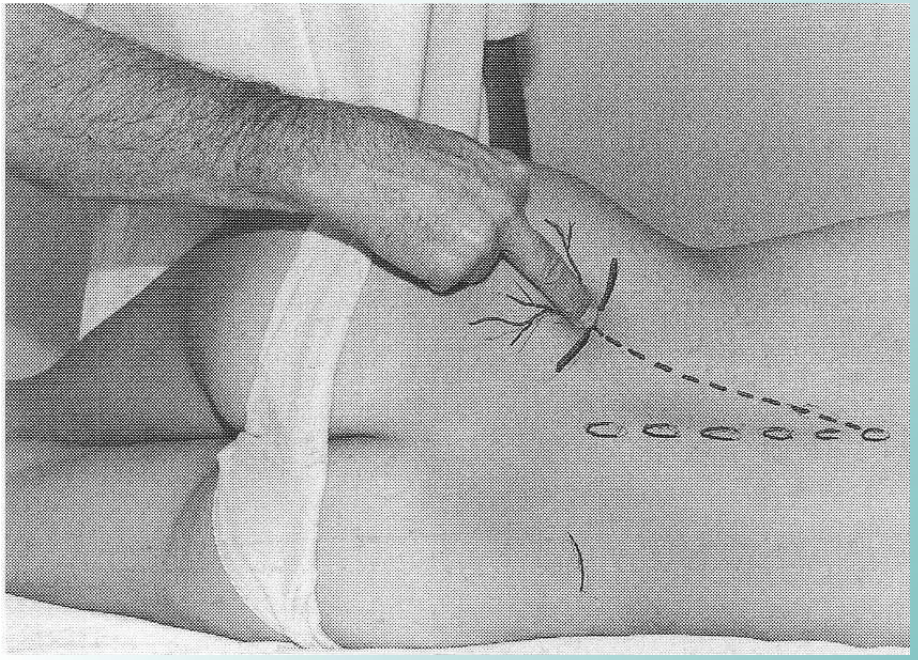


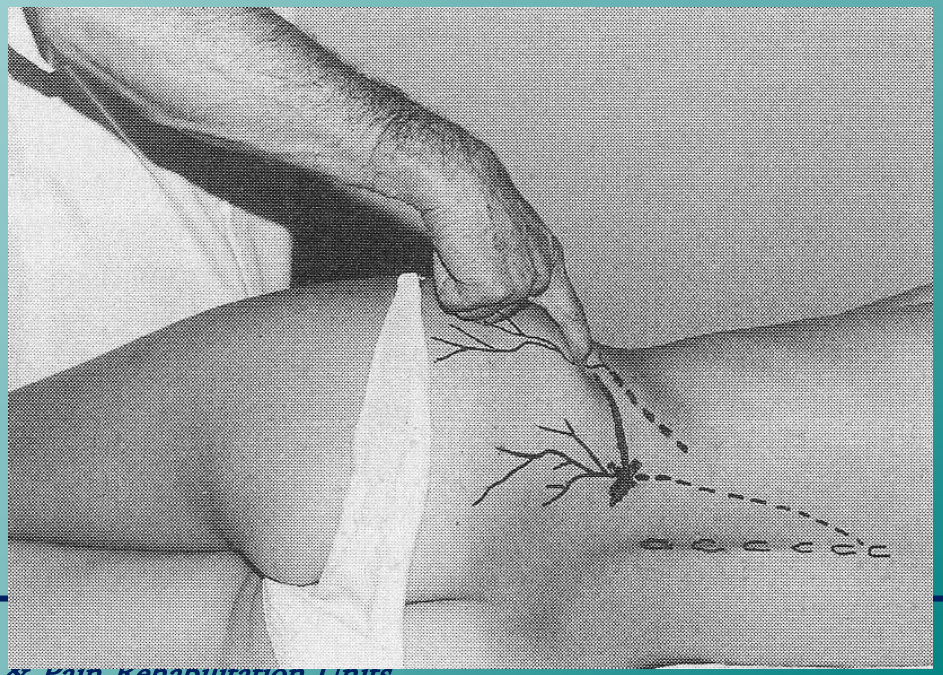


..is not a tendon…

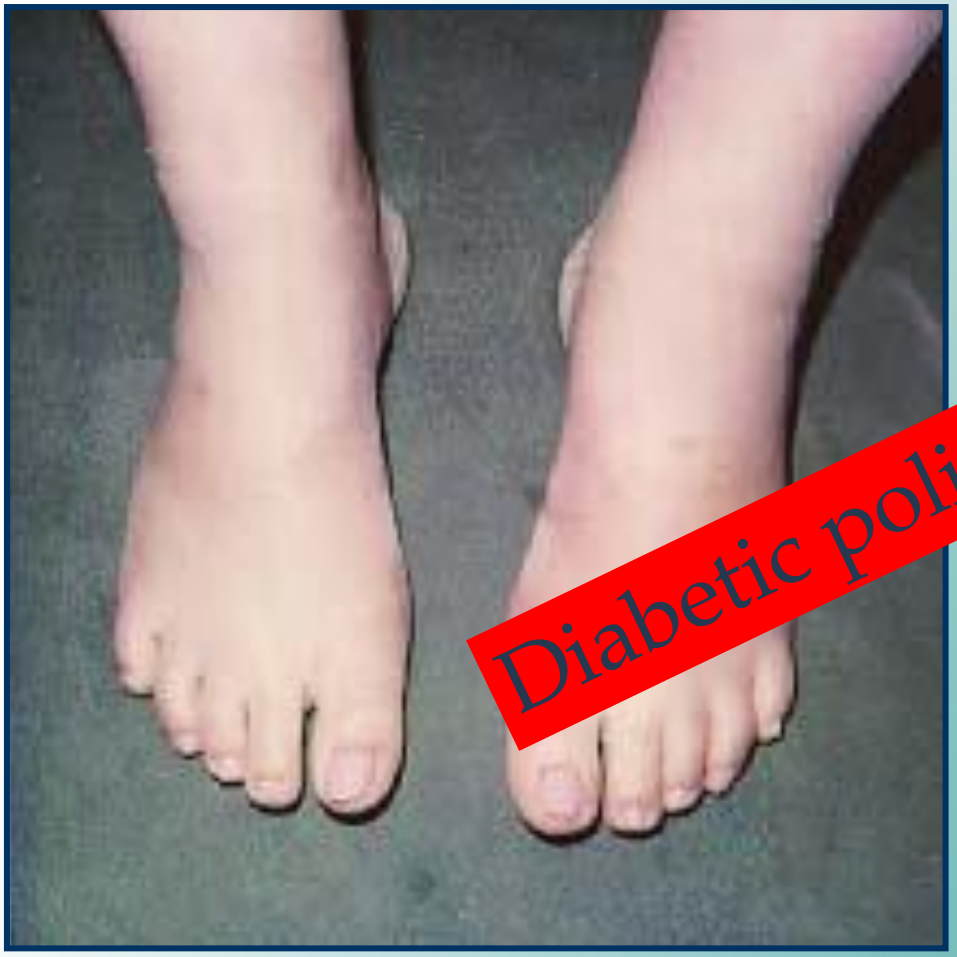


Is not a nerve





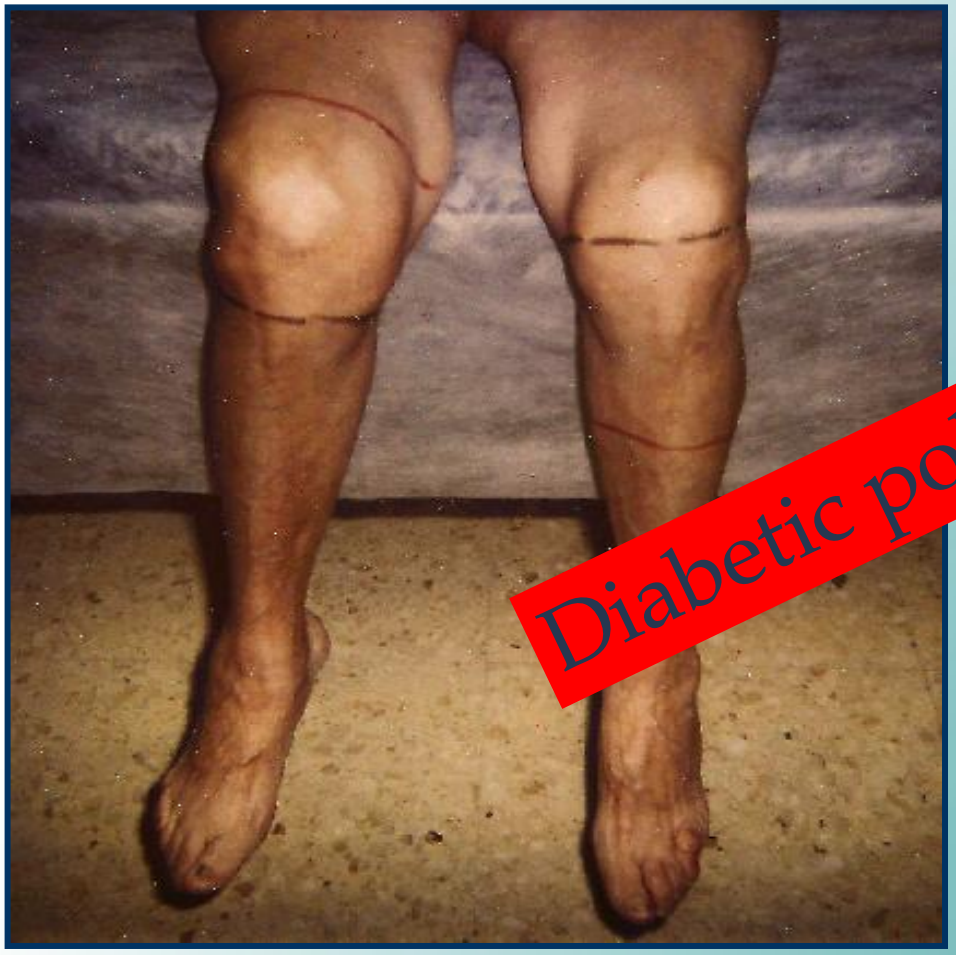
Different disease or mechanisms



Diabetic polineuropathy

- Female, 56 years old
- Reflexes present
- Burning
- Hypertermia, eritema
- Static mechanic hyperalgesia
- Heat hyperalgesia
- No dysestesias

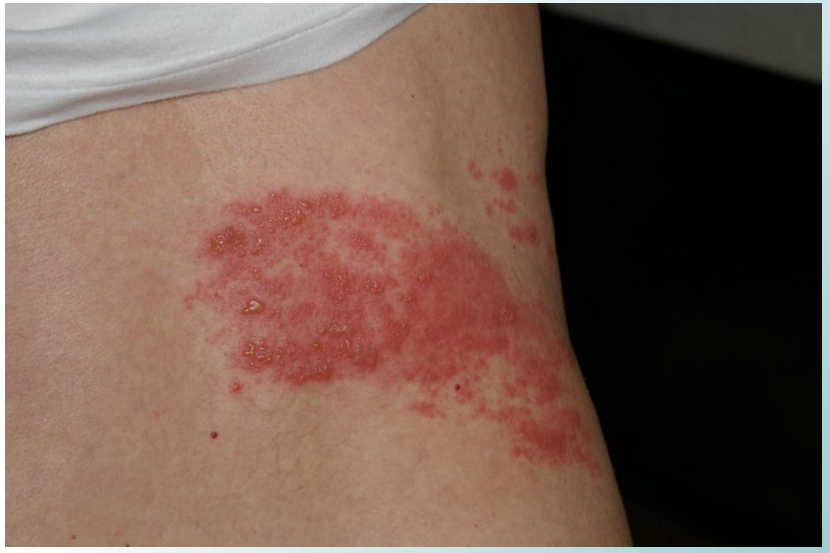
Different disease or mechanisms



Diabetic polineuropathy

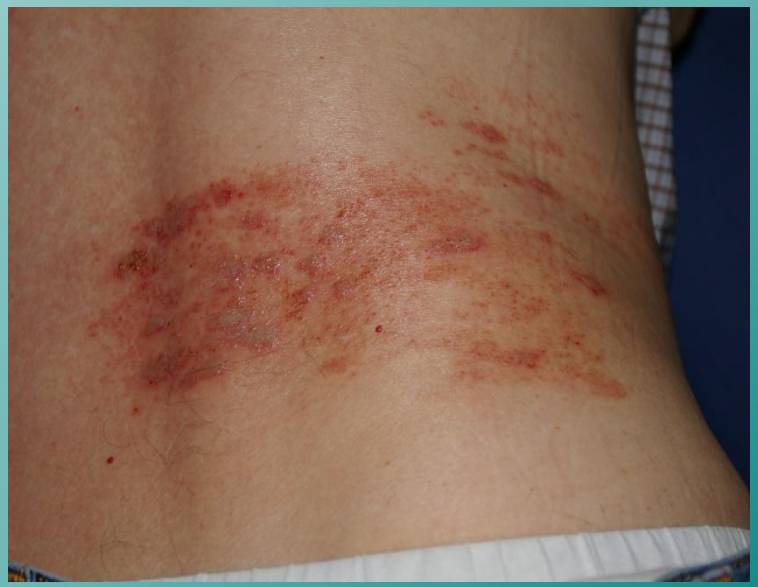
- Male, 70 years old (Mr R.M.)
- Riflexes
- ant spontaneous pain (feet & hands)
- Electric shock-like pain
- Cold skin
- No evoked sensory abnormalities

Same disease, different mechanisms

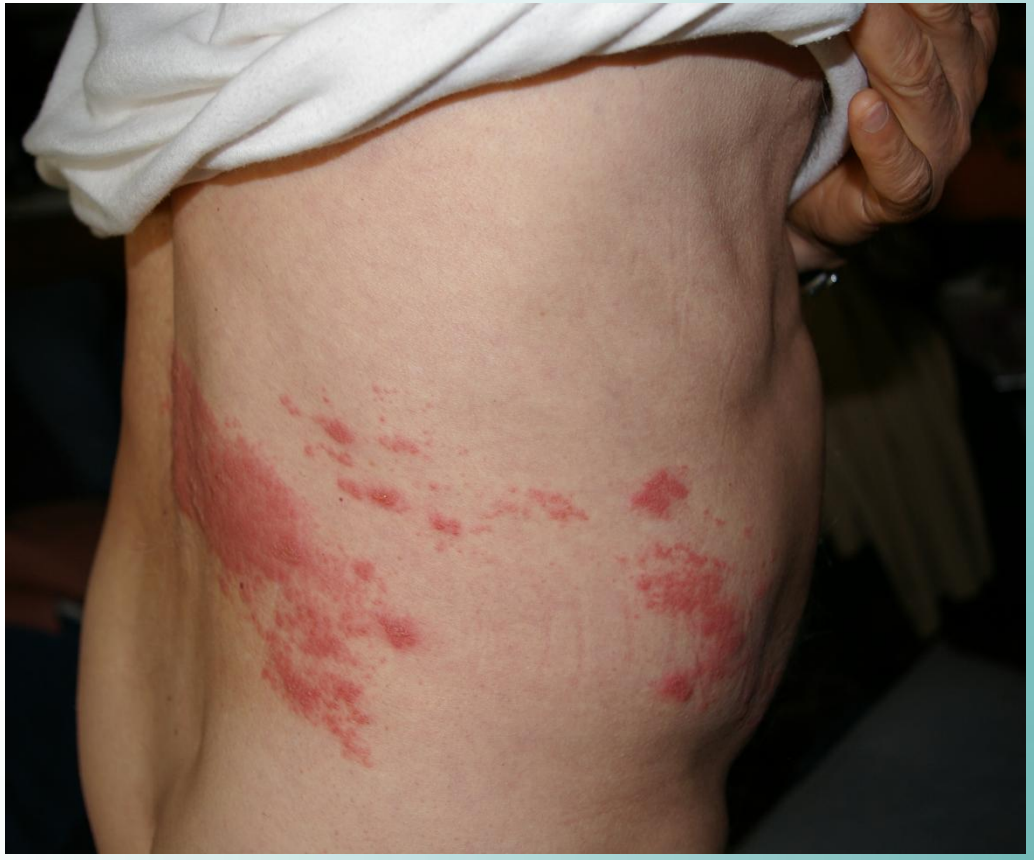


A given patient may have several kinds of abnormal sensation each mediated by a **separate underlying mechanism**.

C fiber nociceptors in an abnormal sensitized status will respond to noxious heat stimulus with a supernormal discharge clinically described as **hyperalgesia**



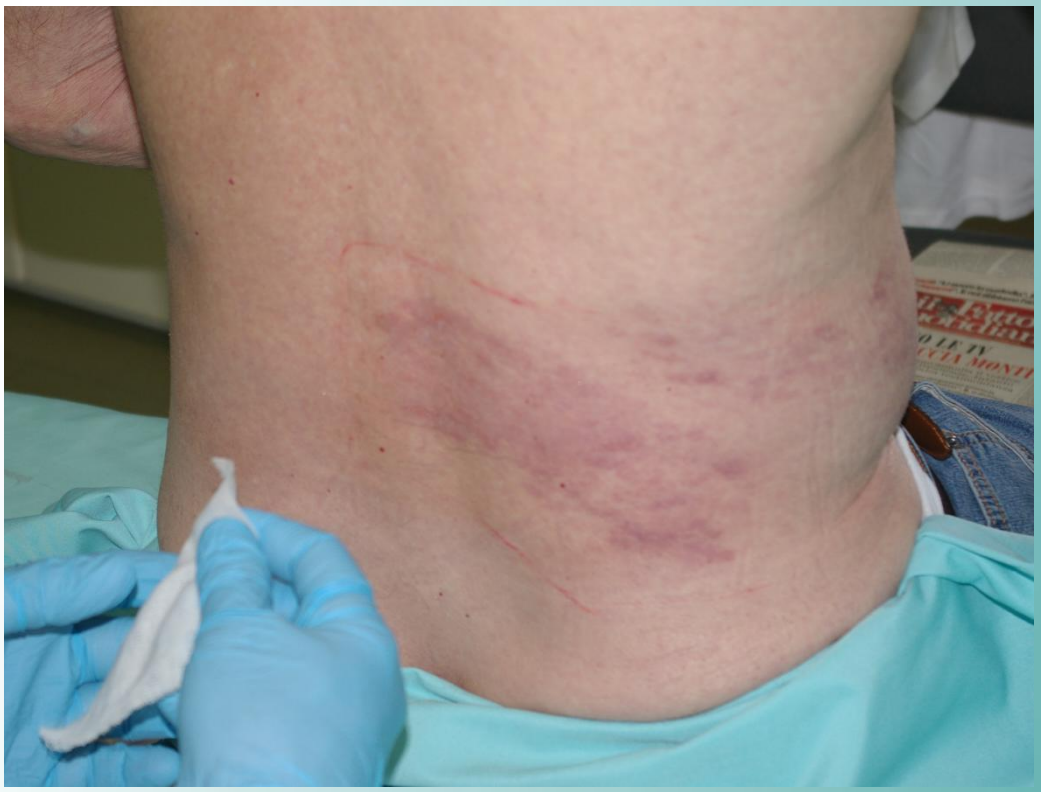
Same disease different mechanisms



- At the same time decrease in C-fiber nociceptors threshold can lead to **static mechanoallodynia**
- and to spontaneous discharge, clinically reported as **spontaneous burning pain**

Same disease, different mechanisms

Moreover the spontaneous, continuous C-nociceptors discharge will evoke **central sensitization** via activation of spinal NMDA receptors.



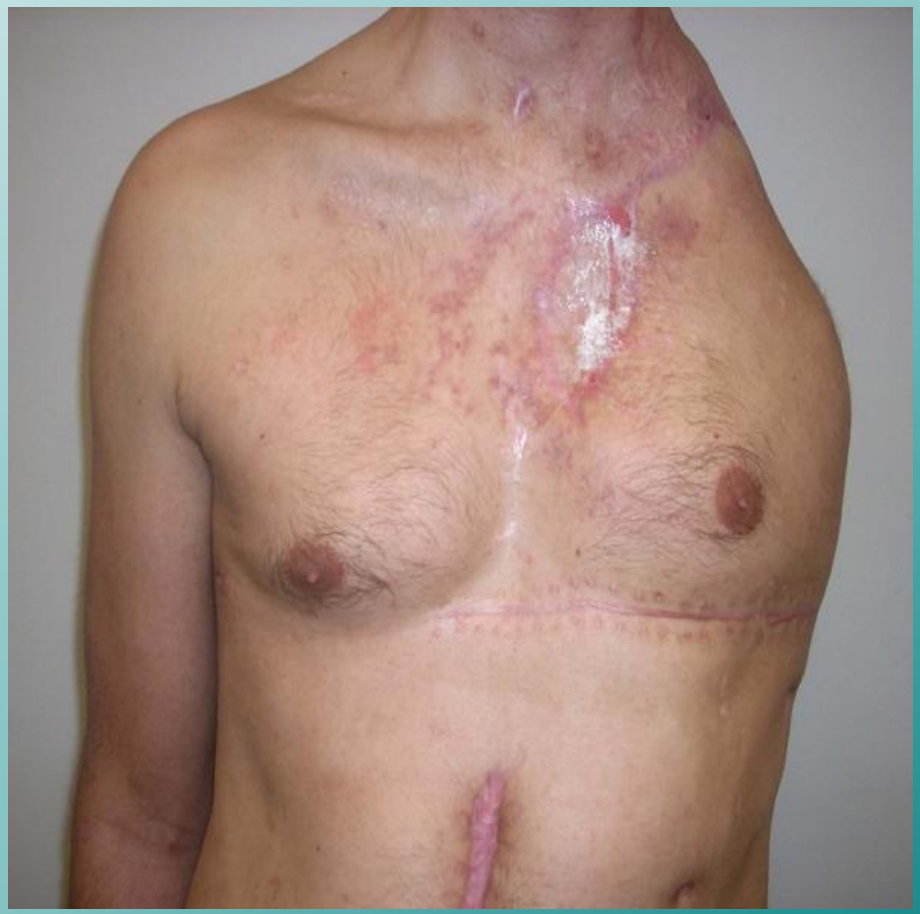
In turn this will lead to the so called **dynamic mechano-allodynia** due to the abnormal processing of normal A-Beta low threshold mechanoreceptors.

Allodynia can happens more easily than one can expect! Nociceptive or neuropathic ?

Same patient , different pains

- Symptoms and signs of neuropathic pain in different diseases overlap considerably

- Multiple pathophysiological mechanisms are responsible for different types of neuropathic pain in a single disease or a single patient



Some uncomfortable hints also for therapies

- Patients affected by the same disease can respond quite differently to the same treatment (systemic/oral)
- The same drug can be used in different diseases
- The same drug can be useful in the same disease but not necessarily in a different patient

More uncomfortable hints

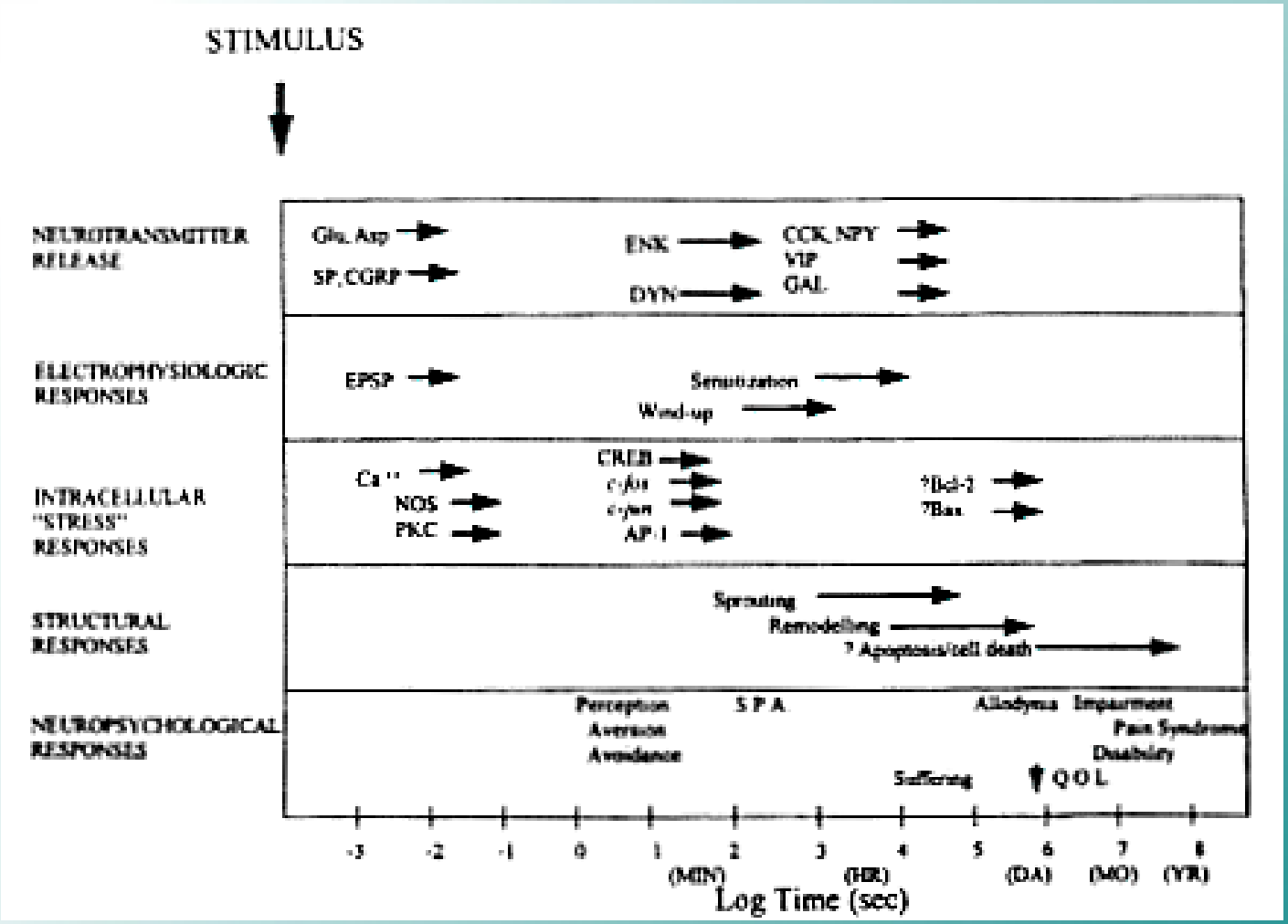
παντα ρει

CRPS (Sudeck, DeTakats & Bonica) classically evolves in three phases

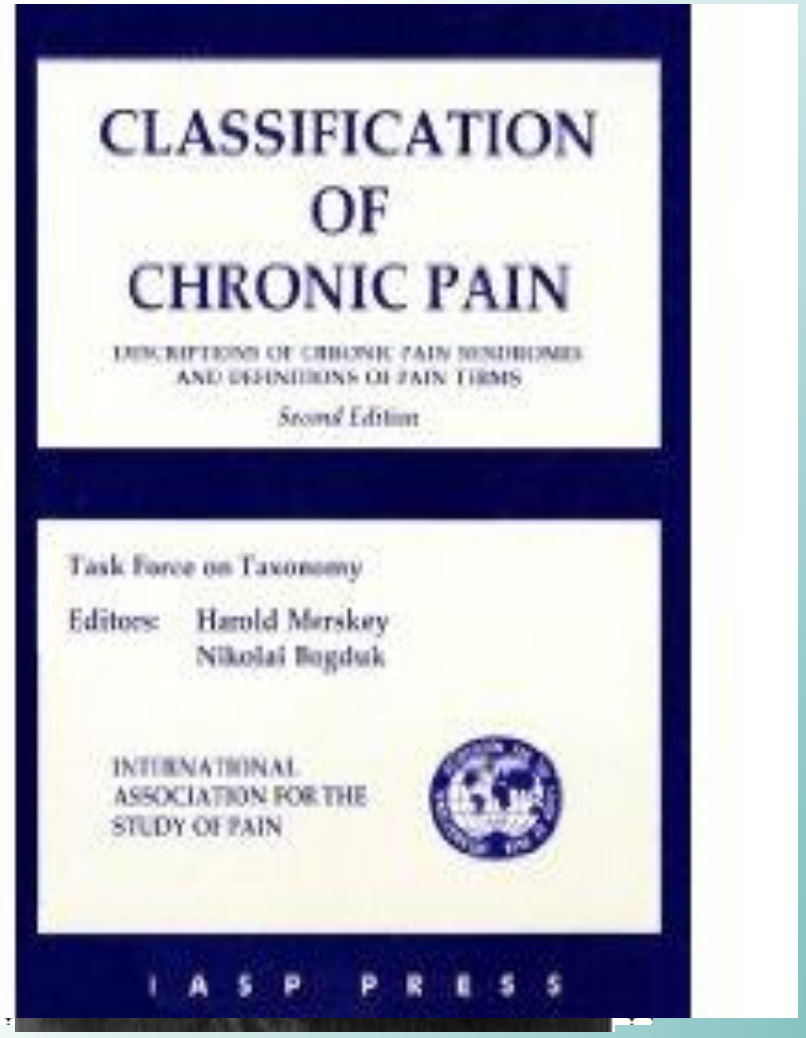
- **Heilentzundung**
- **Dystrophie**
- **Atrophie**

- Mechanisms can change over time.
- Symptoms can also change over time. When this happens it means that also mechanisms are changed.

NeP is a continuum of different clinical pictures in a single disease or a single patient

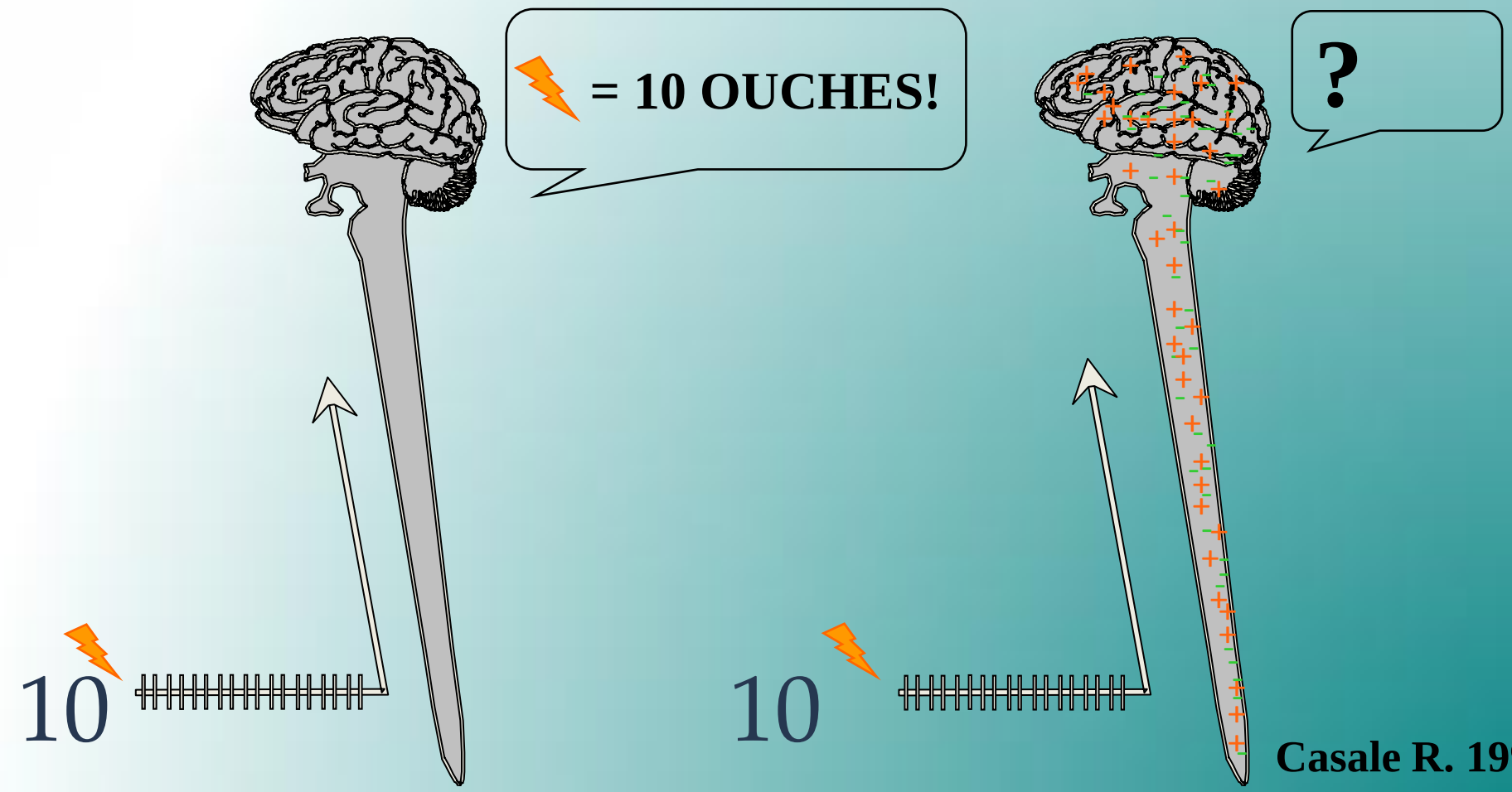


NO brain no pain



- In the IASP supermarket catalog of pains, there are a huge number of pains for each single body segments, however the pain is always elsewhere…

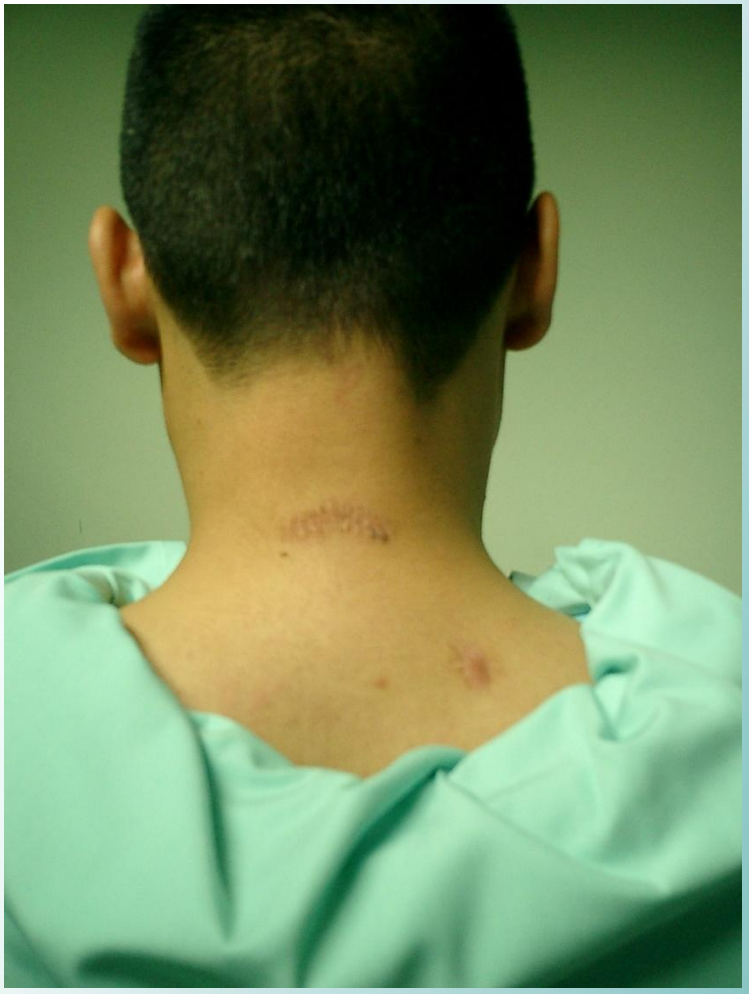
The variable link



Casale R. 1995

Not always seeing is believing

(better if you touch)



Pain: Definition

- Pain, according to the International Association for the Study of Pain (IASP)
  - "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"[1]
- **Pain as disease**
  - **Chronic pain is not simply acute pain that lasts longer. It is a disease process with different mechanisms[2]**
  - Understanding of the mechanisms or pathophysiology of chronic pain can guide optimal treatment[3]

1. Merskey H, et al. *Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd ed. 1994:210.
2. Woolf CJ. *Ann Intern Med*. 2004;**140**:441–451.
3. Baron R. *Nat Clin Pract Neurol*. 2006;**2**:95–106.

IASP Definitions 1994/2008

- **Nociception:** the neural processes of encoding and processing noxious stimuli

- **Nociceptive stimulus**: an actually or potentially tissue-damaging event transduced and encoded by nociceptors

- **Dysesthesia**: an unpleasant abnormal sensation, whether spontaneous or evoked

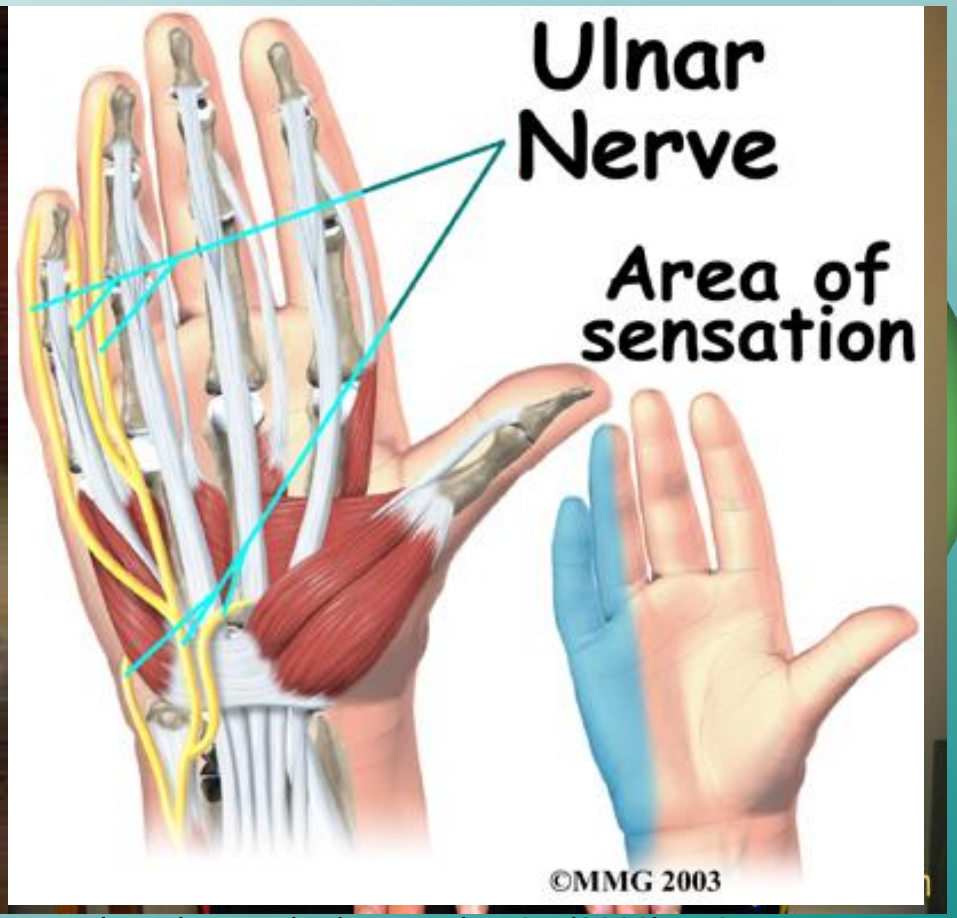
- **Paresthesia**: an abnormal sensation, whether spontaneous or evoked

- **Hyperalgesia**: increased pain sensitivity.

- **Allodynia**: pain in response to a non-nociceptive stimulus.

- **Hyperpathia**: a painful syndrome characterized by an abnormally painful reaction to a stimulus, especially a ripetitive stimulus, as well as an increased threshold

Nociceptive and Neuropathic



1) JD Loeser. And RD Treede The Kyoto protocol of IASP Basic Pain Terminology. Pain 137 (2008) 473–477.
2) Treede RD, Jensen TS, Campbell JN et al. Neuropathic pain. Redefinition and a grading system for clinical and research purposes. Neurology 2008; 70: 1630-1635

Neuropathic Pain
DEFINITION

Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system

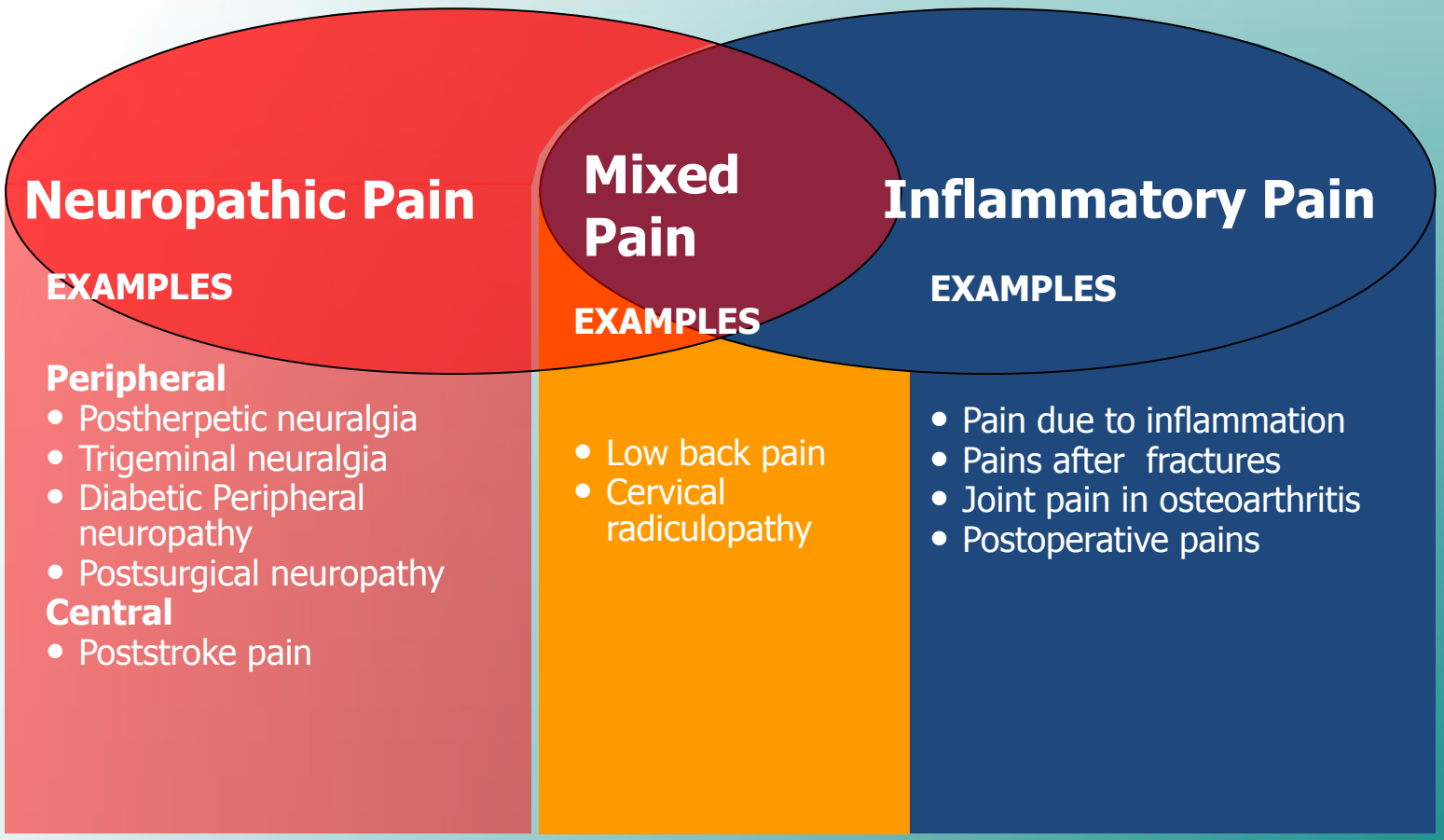
Pain initiated or caused by a primary lesion or dysfunction in the nervous system

Neuropathic pain: Redefinition and a grading system for clinical and research purposes

R. -D. Treede, T. S. Jensen, J. N. Campbell, G. Cruccu, J. O. Dostrovsky, J. W. Griffin, P. Hansson, R. Hughes, T. Nurmikko and J. Serra

Neurology 2008;70;1630-1635; originally published online Nov 14, 2007;

Presentation Across Pain States



EFNS Guidelines, 2003-2004

Neuropathic, Nociceptive (inflammatory) and Mixed Pain

…more space for Mixed forms of pain

Grading System for neuropathic pain

Criteria to be evaluated for each patient

1. Pain with a distinct neuroanatomically plausibile distribution
2. A history suggestive of a relevant lesion or disease affecting thde peripheral or centrali somatosensory System
3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test
4. Demonstration of the relevant lesion or disease by at least one confirmatory test

Definite: all 1 to 4

Probable:1 and 2 plus either 3 or 4

Possible:1 and 2 without conf. evidence from 3 or 4

Unlikely:1 or 2 without conf. evidence from 3 or 4

Working hypothesis: **possibile** neuropathic pain,
if pain distribution is neuroanatomically plausible
and history suggests relevant lesion or disease

NeuPSIG guidelines on neuropathic pain assessment

Maija Haanpää [a,b,*], Nadine Attal [c,d], Miroslav Backonja [e], Ralf Baron [f], Michael Bennett [g], Didier Bouhassira [c,d], Giorgio Cruccu [h], Per Hansson [i], Jennifer A. Haythornthwaite [j], Gian Domenico Iannetti [k], Troels S. Jensen [l], Timo Kauppila [m,n], Turo J. Nurmikko [o], Andew S.C. Rice [p], Michael Rowbotham [q], Jordi Serra [r], Claudia Sommer [s], Blair H. Smith [t], Rolf-Detlef Treede [u]

Confirmatory tests:

a: Negative or positive sensory signs, confined to innervation territory of the lesioned nervous structure

b: Diagnostic test confirming lesion or disease explaining neuropathic pain
e.g. ENMG to show the peripheral nerve lesion
e.g. MRI to show the central nervous system lesion

neither → **Unconfirmed** as neuropathic pain

one → **Probable** neuropathic pain

both → **Definite** neuropatic pain

Neuropathic Pain

Unfamiliar symptoms
No tissue alteration? Dystrophic
Sensory, Motor, Autonomic signs

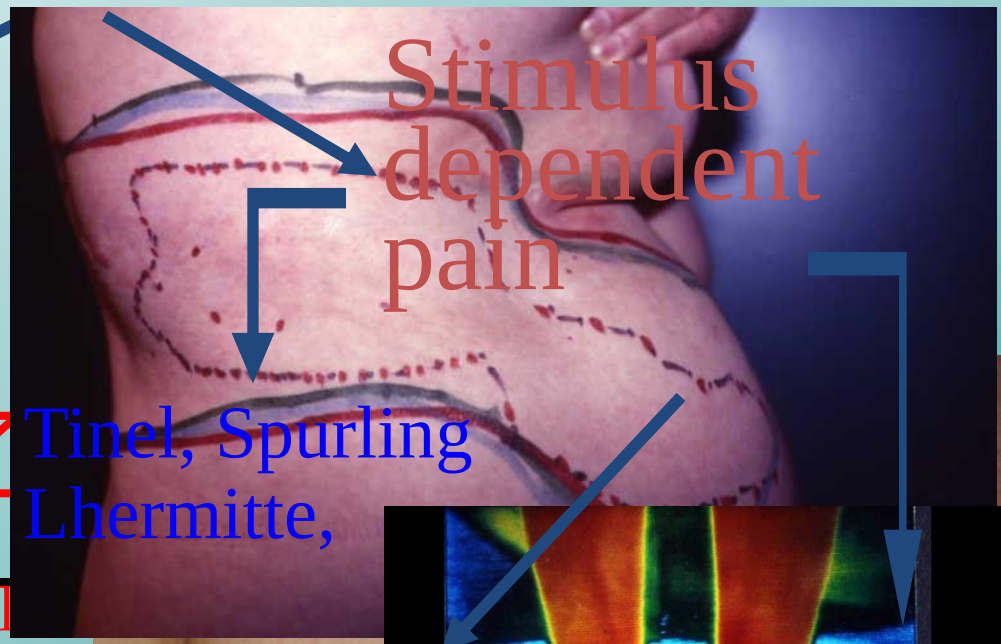
Spontaneous pain

Continuous **burning**, aching cramping, smarting, dull crushing, sharp

Paroxysmal, lancinating stabbing electric shock-l

Stimulus dependent pain

Tinel, Spurling Lhermitte,



Allodynia

Static mechanical

Dynamic mechanical

PHN, Central Pain Diabetic Neuropathy

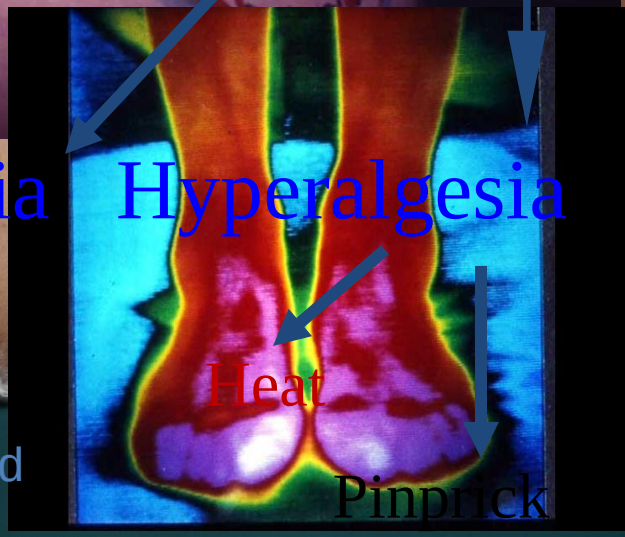
Warmth

Cold

Hyperalgesia

Heat

Pinprick



N. Attal et al. Neuropathic pain: are there distinct subtypes depending on the aetiology or anatomical lesion? Pain 138 (2008) 343-353

Chronic pain as a disease in its own right

Pain as a warning system

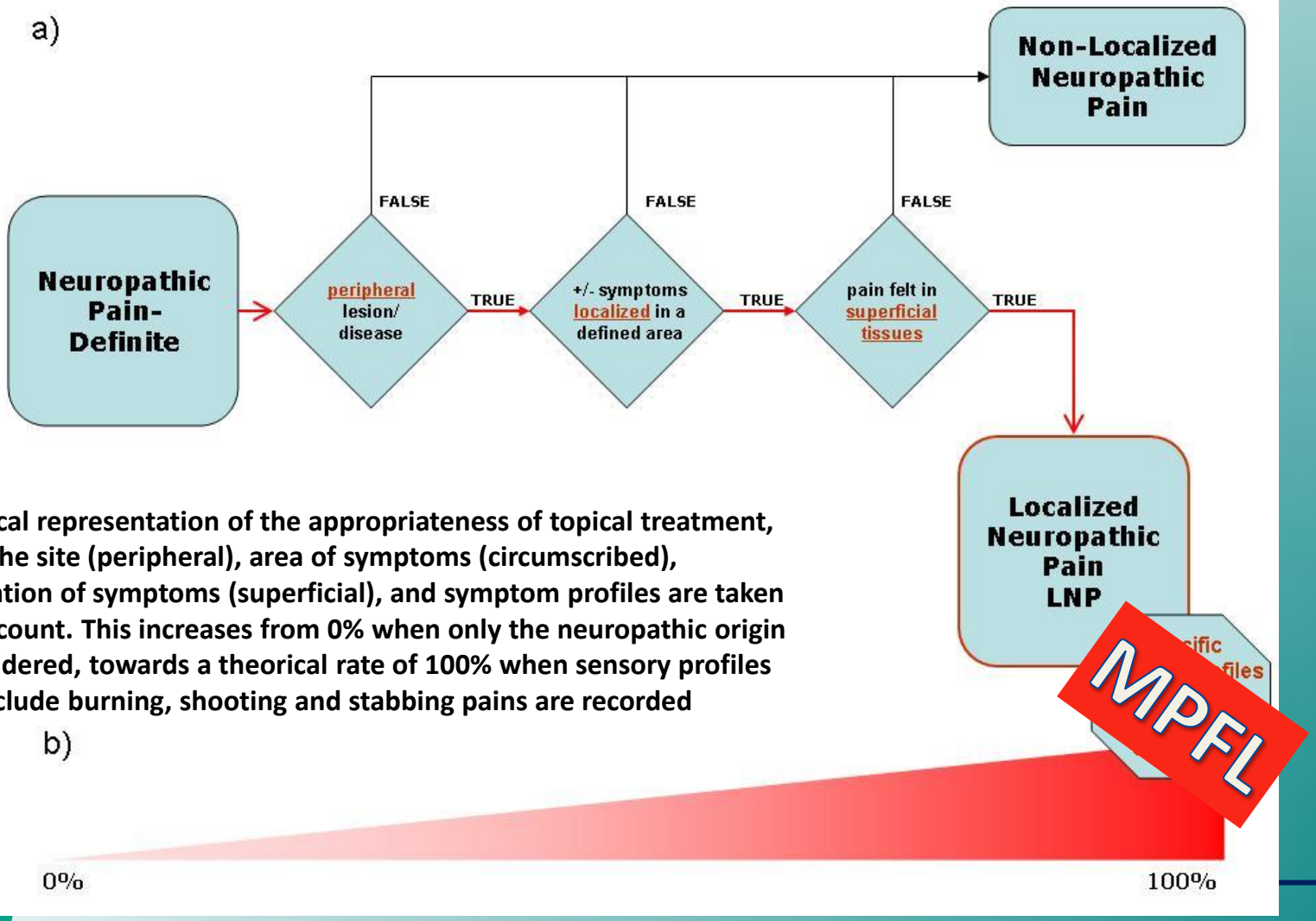
Pain → acute / chronic

Temporal parameter

In the shaded boxes are reported some of the most intriguing clinical pictures where the nociceptive/neuropathic and peripheral/central origin is still matter of controversies.

- **NOCICEPTIVE**
  - localized
  - diffuse → CWP, FIBRO
- **NEUROPATHIC**
  - CENTRAL → diffuse → CWP, FIBRO, CRPS I/II
  - PERIPHERAL → diffuse → CRPS I/II
  - **localized** → LNP
- **MIXED**
  - CONCOMITANT (Time/NO Side)
  - SUPERIMPOSED (Side/NO Time)
  - MIXED (Time/Side/Neurop+Nocicept.)

The algorithm (Casale& Mattia, 2014)



Graphical representation of the appropriateness of topical treatment, when the site (peripheral), area of symptoms (circumscribed), localization of symptoms (superficial), and symptom profiles are taken into account. This increases from 0% when only the neuropathic origin is considered, towards a theorical rate of 100% when sensory profiles that include burning, shooting and stabbing pains are recorded

DN4 Questionnaire

Please complete this questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

	yes	no
1 - **Burning**		
2 - **Painful cold**		
3 - **Electric Shocks**		

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

	yes	no
4 - **Tingling**		
5 - **Pins and Needles**		
6 - **Numbness**		
7 - **Itching**		

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

	yes	no
8 - **Hypoesthesia to touch**		
9 - **Hypoesthesia to prick**		

Question 4: In the painful area, can the pain be caused or increased by:

	yes	no
10 - **Brushing**		

PAIN

Pain 114 (2005) 29–36

www.elsevier.com/locate/pain

Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4)

Didier Bouhassira[a,*], Nadine Attal[a], Haiel Alchaar[b], François Boureau[c], Bruno Brochet[d], Jean Bruxelle[e], Gérard Cunin[f], Jacques Fermanian[g], Patrick Ginies[h], Aurélie Grun-Overdyking[i], Hélène Jafari-Schluep[i], Michel Lantéri-Minet[b], Bernard Laurent[j], Gérard Mick[k], Alain Serrie[f], Dominique Valade[f], Eric Vicaut[l]

A total score of 4 out of 10 or higher suggest Neuropathic Pain

The DN4 showed

83% sensitivity and

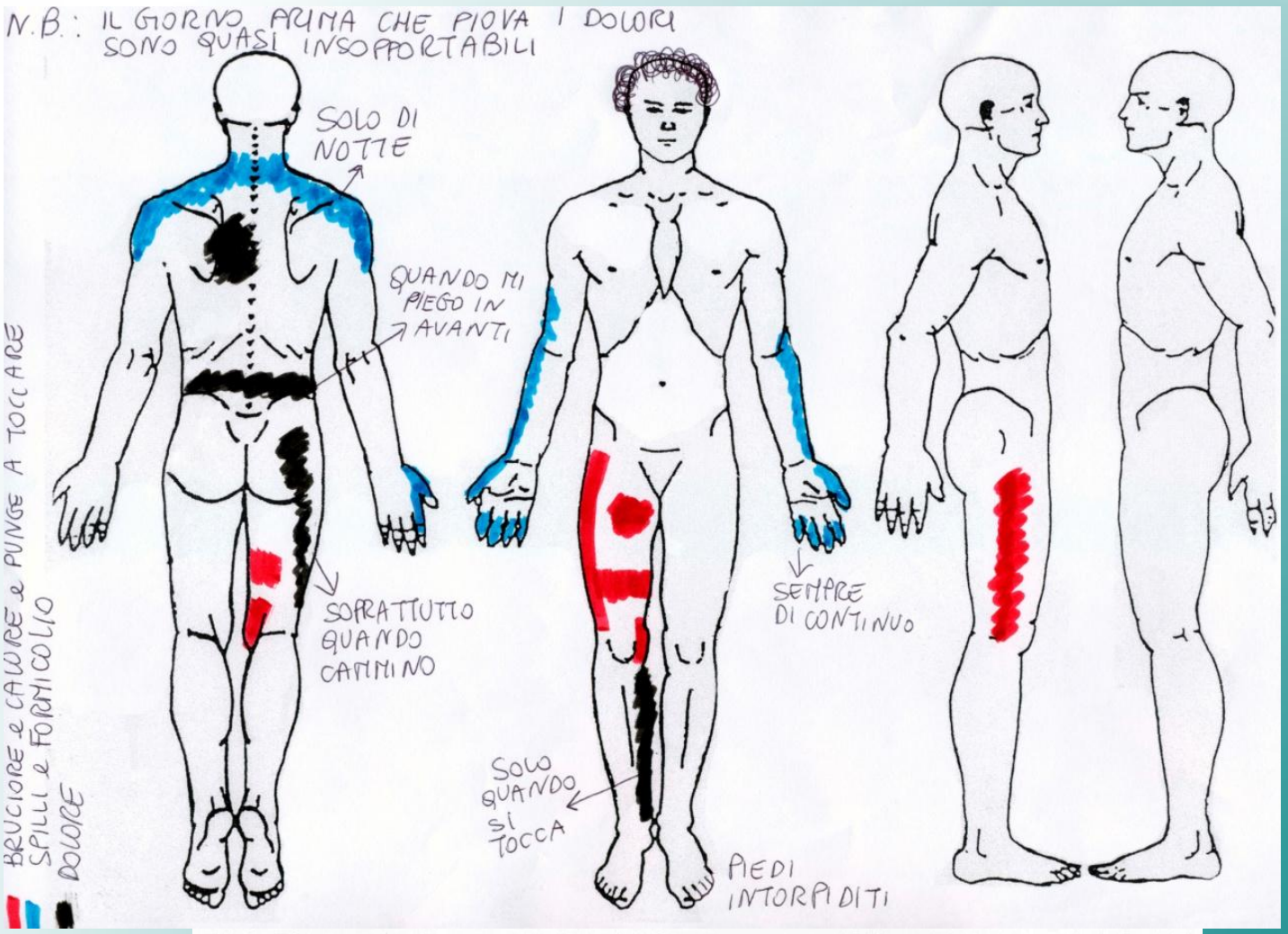
90% specificity

compared to clinical diagnosis in the development study.

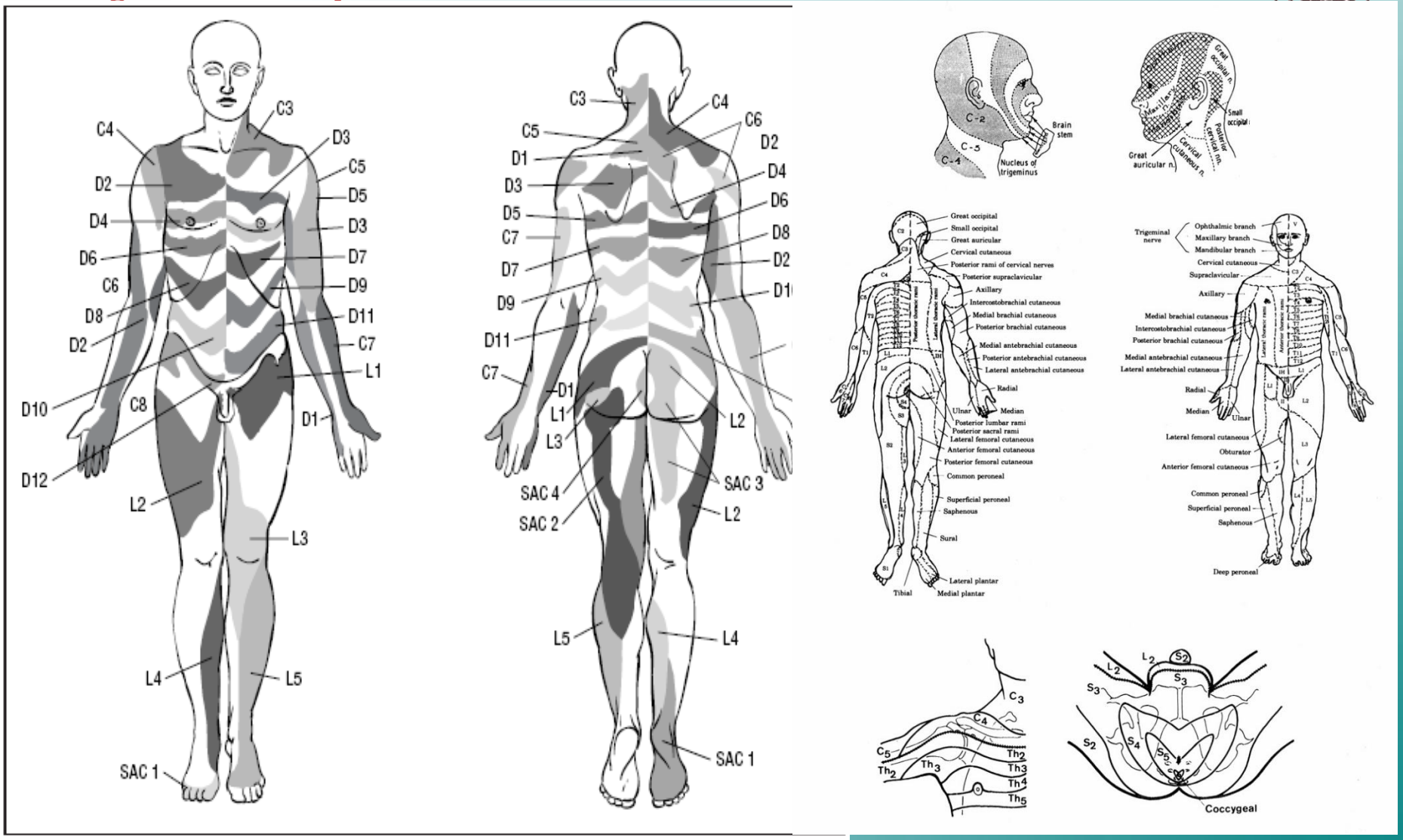
PAIN DISTRIBUTION

Cartography, topography and pain drawing

Pain drawing by the patient

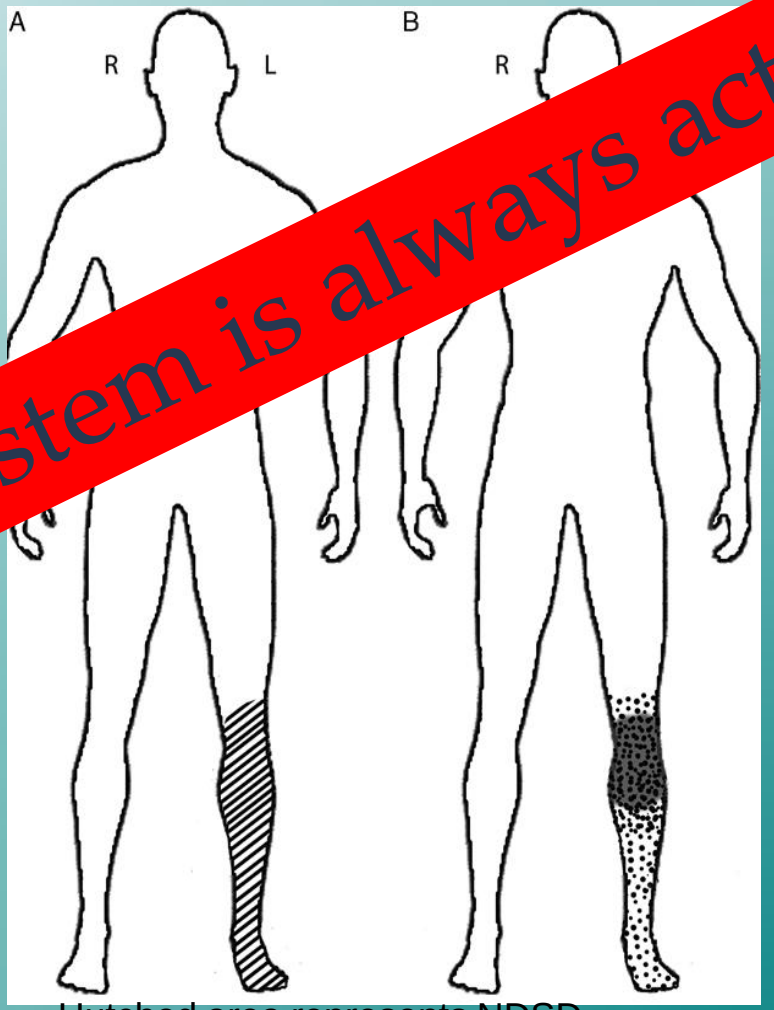


In 1900 Head &Campbell "The Pathology of Herpes Zoster and Its Bearing on Sensory Localization"



A 37-years-old male suffered peroneal nerve injury 19 years before consultation as a complication of a knee surgery. This left him with a severe drop foot (for which he had tendon transfer) and ananesthetic but painless leg from the knee to the foot. Despite his painless drop foot, he managed to work for years wearing a drop foot brace as a postal worker.

- **Sixteen years later (December 1997), he suffered a twisting left knee injury associated with onset of sharp knee pain and within afew weeks he noted return of sensation, strength, and ankle movements in his left leg.**
- **In May 2000, the left knee was cold and purplish with visible quad atrophy and hypersensitivity to pinprick and touch across the knee and leg and some hypoesthesia below the knee.**
- **Electrophysiological studies showed old, par… recovered peroneal nerve injury. Under… amytal,he experienced remarkable… allodynia but persistence of pi… (a typical response for neur… , reported in Mailis et al 1997)**
- **Th… II was made. Although the patient …g "always a cold but painless knee since …e kept asking if "we could give him back the …ic leg that he had for 16 years," as he did not …d the anesthesia and severe weakness but he did mind the pain! He failed to respond to neuropathic adjuvant medications or opioids and went on long-term disability.**



Hutched area represents NDSD, shaded area pain, dotted area dysesthesiae.

Modifications in the sensory-motor cortical organization are extraordinarily fast and they have been perceived at least ones in our daily life

PAIN SCHOOL

HABILITA
CARE & RESEARCH REHABILITATION HOSPITALS

Habilita, Advanced Technology & Pain Rehabilitation Units

It could has been worst that this