



Assessment of Neuropathic Pain

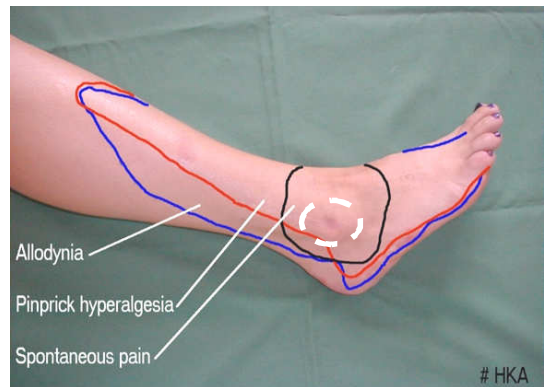
Workshop Hong Kong Pain Society
Queen Elizabeth Hospital April 23, 2010



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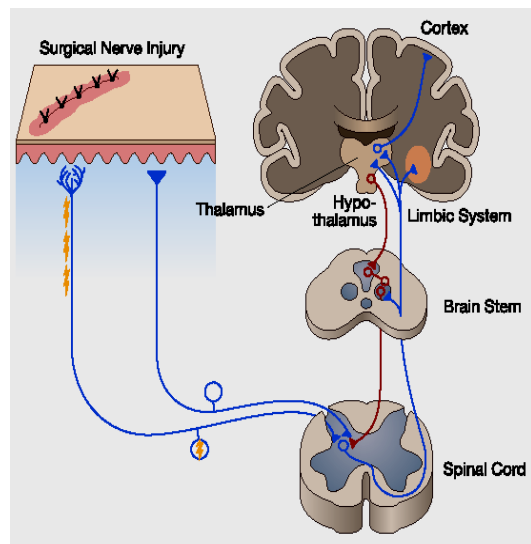
Peripheral Neuropathic Pain case

- 42 yr. old F
- Tibial fracture 1996
- 1996 removal of ostesynthesis
- 1998 removal of neuroma peronal nerve
- Constant burning pain in malleol area
- Evoked pain in lower leg and foot
- VAS pain: 5-10

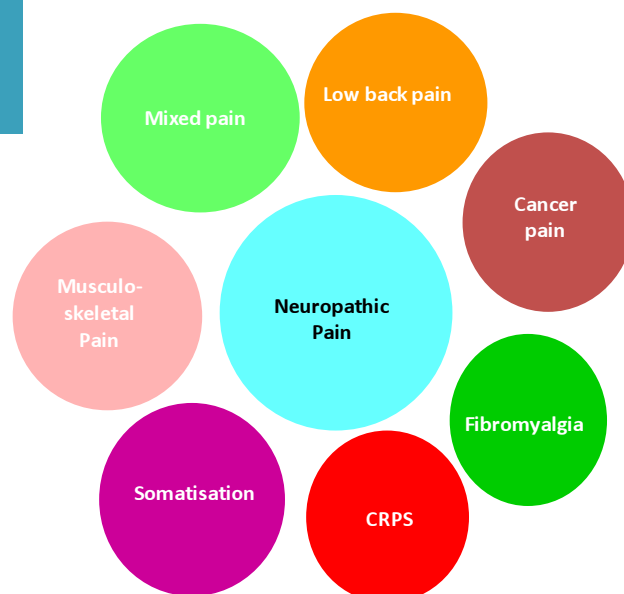


Characteristics

- Sensory loss
- Spont + evoked pain
- Allodynia/hyperalgesia
- Specific sensory pattern
- Paroxysms
- Aftersensations
- Abnormal summation



Neuropathic Pain = Pain initiated or caused by a primary lesion, dysfunction or transitory perturbation of the peripheral or central nervous system (IASP, 1994)



Neuropathic Pain = Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system (Treede et al. Neurology 2008).

Neuropathic Pain: Definitions

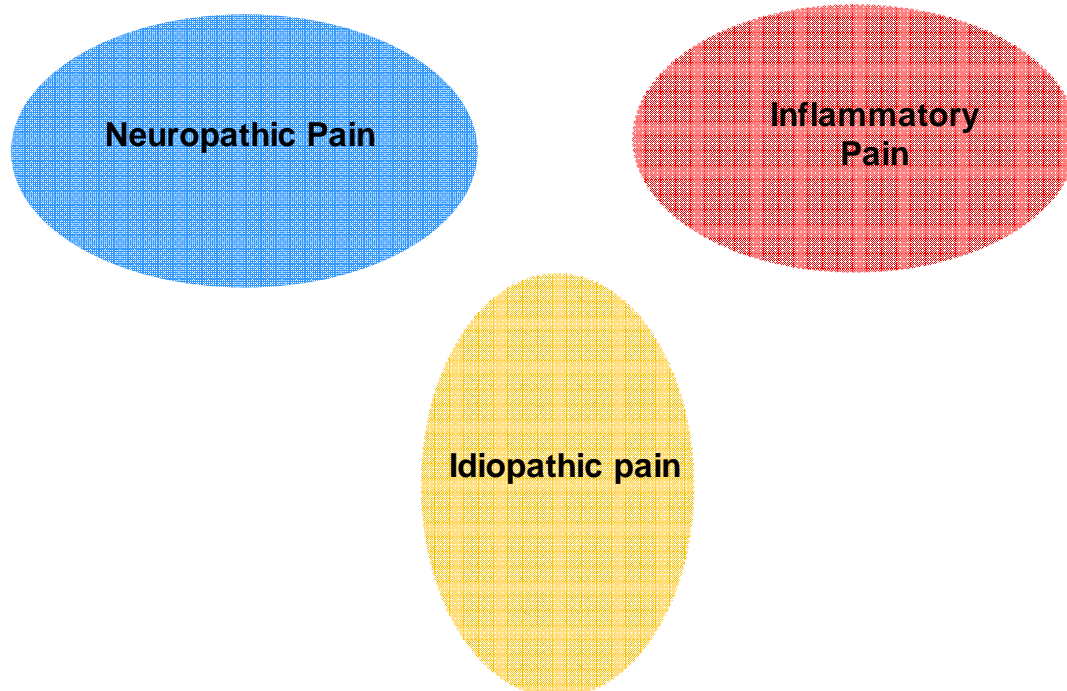
Symptom/Sign	Description
Spontaneous symptoms	
– Spontaneous pain	Persistent burning, intermittent shock-like or lancinating pain
– Dysesthesias	Abnormal unpleasant sensations e.g. shooting, lancinating, burning
– Paraesthesias	Abnormal, not unpleasant sensations e.g. tingling
Evoked symptoms	
-- Par/dysesthesia	Abnormal, (un)pleasant sensations e.g. tingling
– Allodynia	Painful response to a non-painful stimulus e.g. warmth, cold, pressure, stroking
– Hyperalgesia	Increased response to a painful stimulus e.g. pinprick, cold, heat
– Hyperpathia	Delayed, explosive response to a painful stimulus

Chronic Pain: Classification

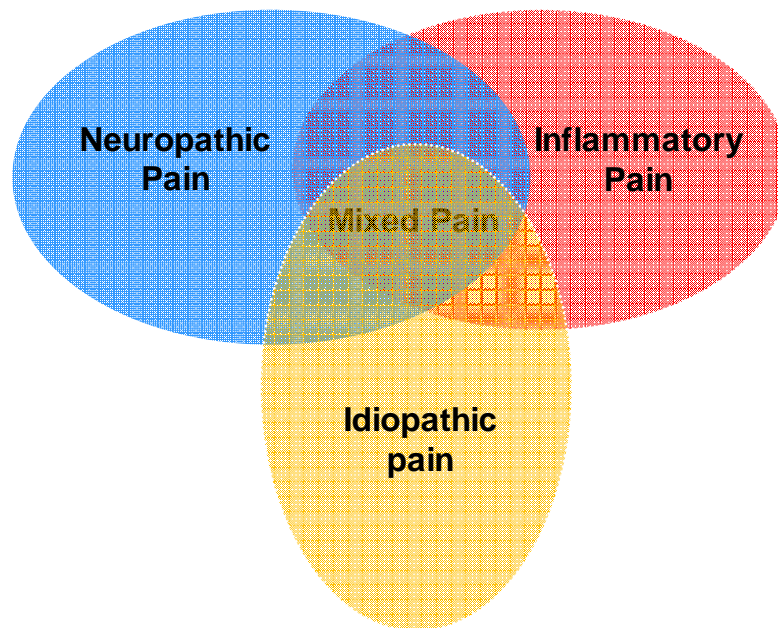
Neuropathic	Nociceptive	Mixed Pain	Idiopathic Pain
Nerve injuries	Osteoarthritis	Cancer Pain	Fibromyalgia
Amputations	Rheum. arthritis	Neck pain	Bodyly distress
Plexus avulsion	Postop pain	Low Back pain	Whiplash injury
PHN	Colitis	Limb Pain	Irrit. bowel disease
Trig. neuralgia	Tendinitis	Visceral pain	Interstitial cystitis
Neuropathies	Myositis	Thoracic pain	
Syringomyelia	Migraine ?		
MS	CRPS ?		
Spinal cord injury			
Stroke			
CRPS ?			
Other			

Woolf 2004
Finnerup & Jensen 2005

Chronic pain: Classification (“splitting”)



Chronic pain: Classification (“lumping”)



Peripheral Neuropathic pain: Diagnostic methods

- History
 - Neurological exam incl. Sensory exam.
 - Neurography
 - Quantitative sensory testing (QST)
 - Challenging stimulus (capsaicin/heat/cold)
 - Microneurography, EMG
 - Imaging (X-Ray, CT, MRI, fMRI, PET EEG)
 - Nerve/skin biopsies, surgical exploration
 - Pharmacological trials
- } Basic (clinical)
- } Special (research)

Bedside tests:

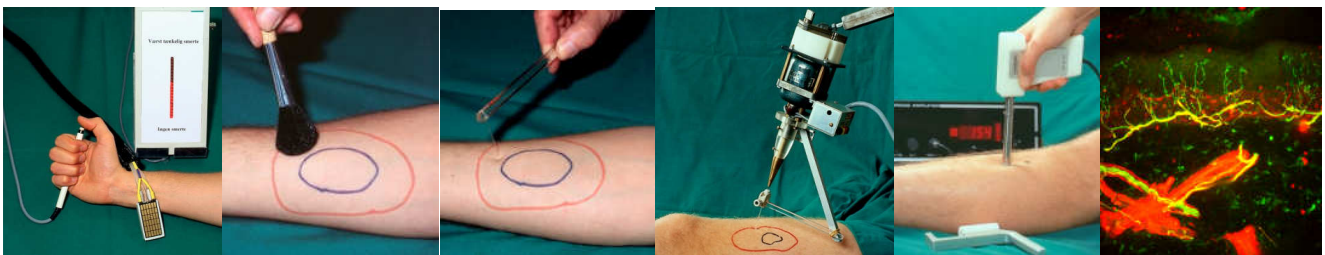
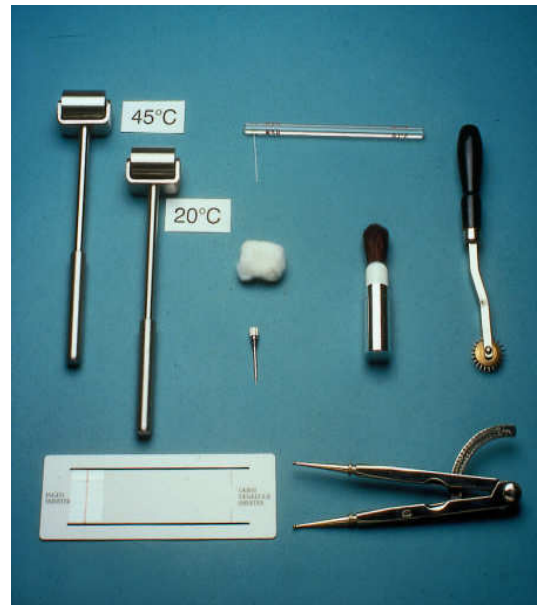
Thermal, touch, brush,
pinprick, pressure,
TP discrimination

Record:

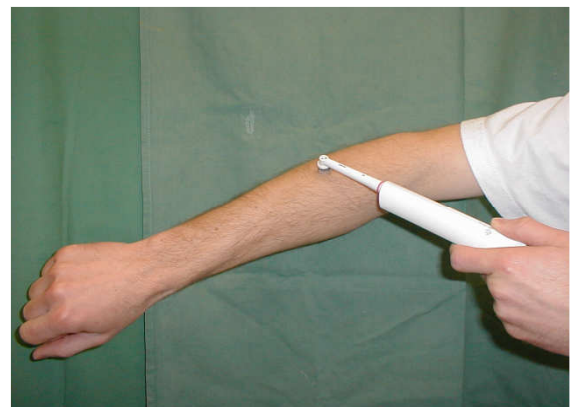
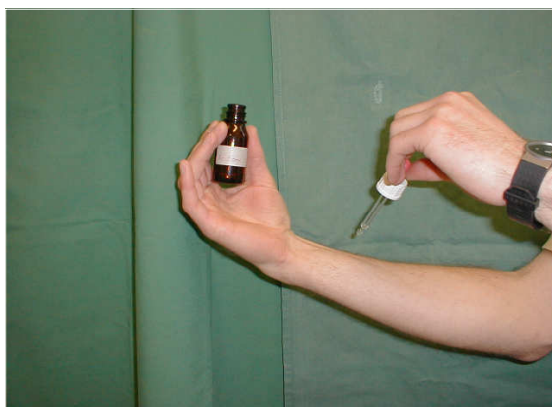
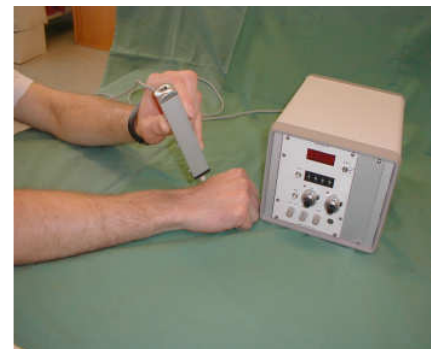
Normal
reduced
increased

Specific tests (QST):

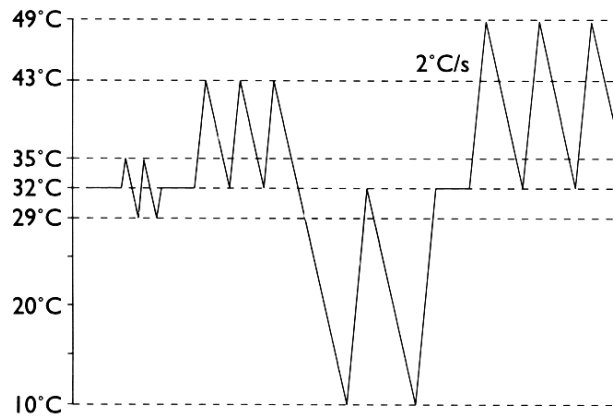
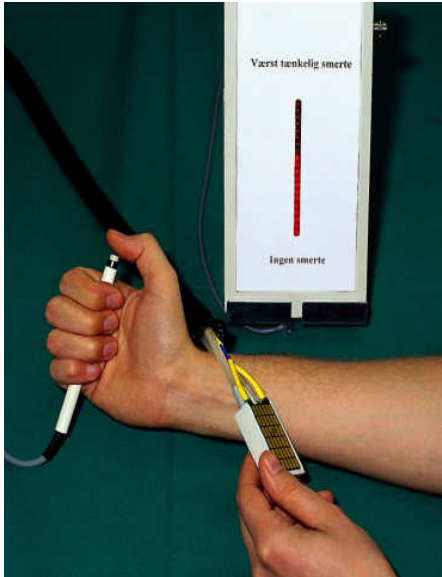
Thermo, brush area
pinprick area, algometry
Skin biopsies



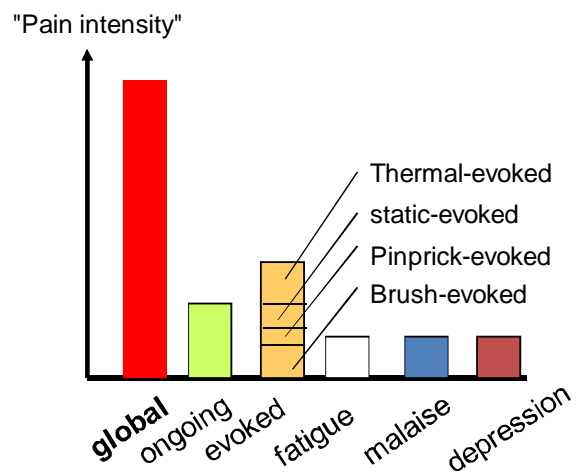
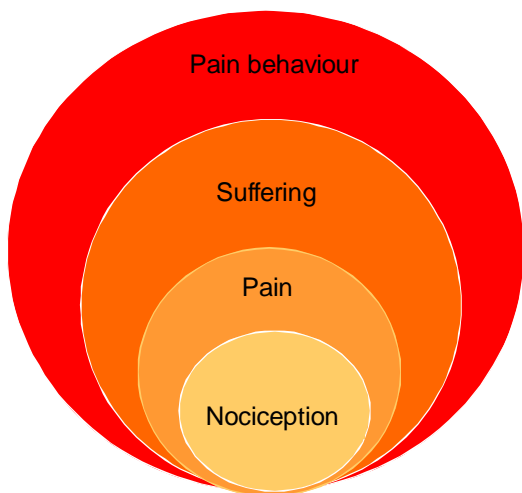
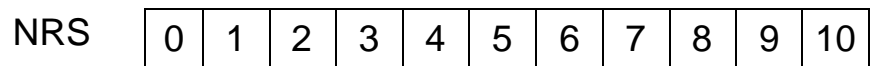
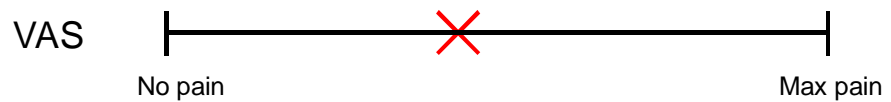
Quantitative sensory testing:



Thermo-testing

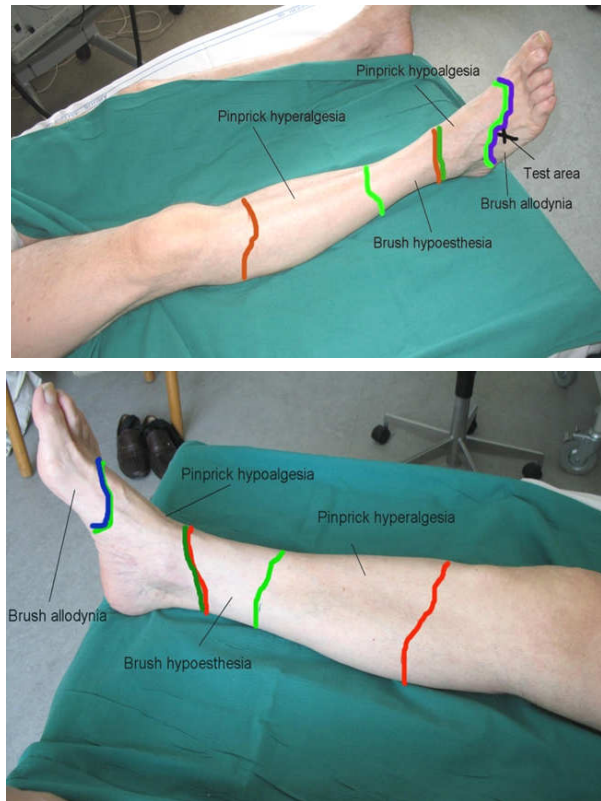


Chronic Pain: Assessment of Pain



Small fibre neuropathy

- 77 yr., M
- Prior history of Pagets disease and coronary heart disease
- For 2 yrs. burning smarting pains in feet. Pain provoked by walking.
- Normal muscle function. Tendon reflexes all normal
- Reduced sensitivity to pinprick and cold form ankle and distally
- Normal sensitivity to touch vibration and position



Small fibre neuropathy

77 yr old male

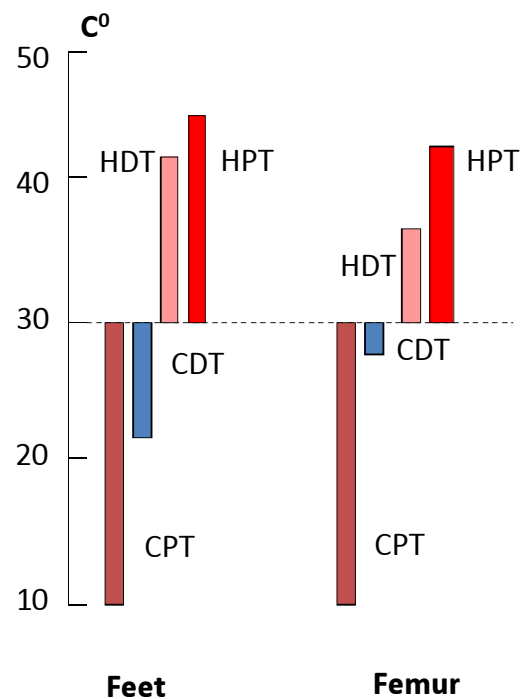
Mechanical sensitivity

	Feet	Femur
Tactile Det Thresh	0.7 g	0.7 g
Tactile Pain Thresh	76g	446g
Pres Pain Thresh	252 kPa	246kPa
Pres Toll Thresh	407 kPa	312 kPa

Summary:

Reduced pin prick treshhold
Reduced thermal detect. threshold

Thermal sensitivity



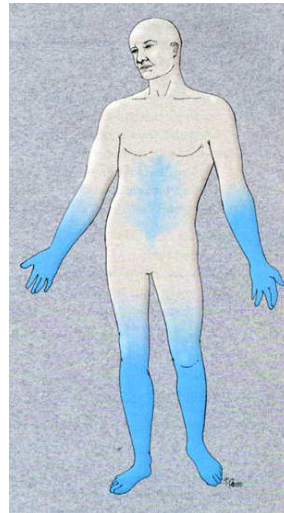
NP Grading system: Criterion 1

1. Pain with a distinct neuroanatomically plausible distribution.

A region corresponding to a peripheral innervation territory or to the topographical representation of a body part within the CNS.

Pain drawing

Example: Distal sensory neuropathy



Treede, Jensen, Campbell, Cruccu, Dostrovsky, Griffin, Hansson, Hughes, Nurmikko, Serra, *Neurology* (2008)

NP Grading system: Criterion 2

2. A history of a relevant lesion or disease affecting the peripheral or central somato-sensory system.

The lesion or disease is reported to be associated with pain with a temporal relationship typical for the condition.

Medical history

Example:
painful diabetic neuropathy

- 43 yr. old Female
- IDDM for 20 years.
- For 5 years numbness in feet
- Last 4 years burning pain in feet
- Last 2 years tingling in fingertips.

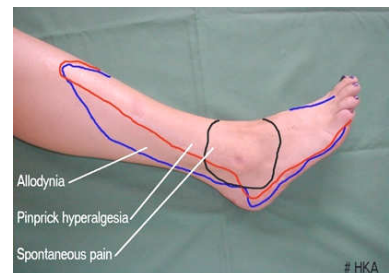
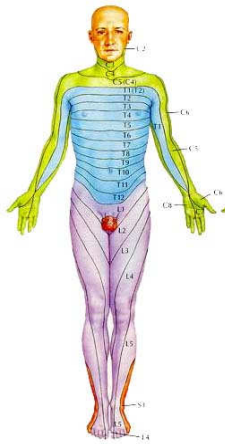
Treede, Jensen, Campbell, Cruccu, Dostrovsky, Griffin, Hansson, Hughes, Nurmikko, Serra, *Neurology* (2008),

NP Grading system: Criterion 3

3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test.

As part of the neurological examination, these tests confirm the presence of neurological signs concordant with the distribution of pain.

Confirmatory tests:



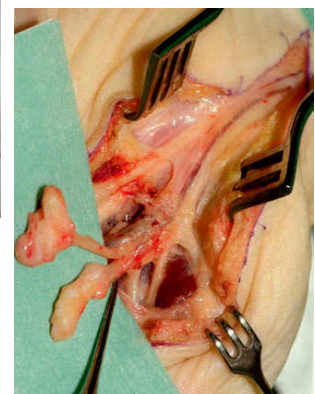
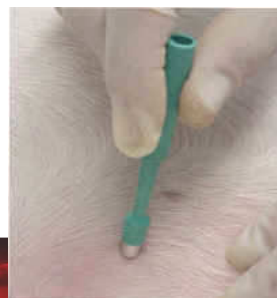
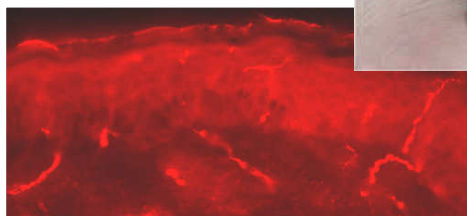
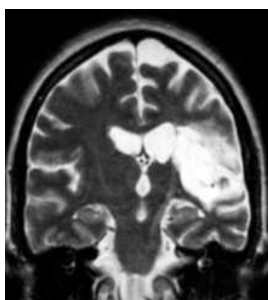
Treede, Jensen, Campbell, Cruccu, Dostrovsky, Griffin, Hansson, Hughes, Nurmikko, Serra *Neurology* (2008)

NP Grading system: Criterion 4

4. Demonstration of the relevant lesion or disease by at least one confirmatory test.

As part of the neurological examination, these tests confirm the diagnosis of the suspected lesion or disease. These confirmatory tests depend on which lesion or disease is causing neuropathic pain.

Confirmatory tests:



Treede, Jensen, Campbell, Cruccu, Dostrovsky, Griffin, Hansson, Hughes, Nurmikko, Serra *Neurology* (2008)

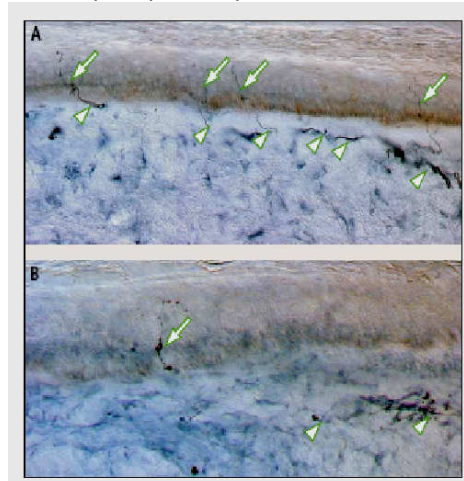
Small fibre Neuropathies: Biopsy

Technique:

3 mm punch skin biopsies
 Sterile condition lidocaine anesthesia
 Immuno staining of 50 µm sections

Markers used:

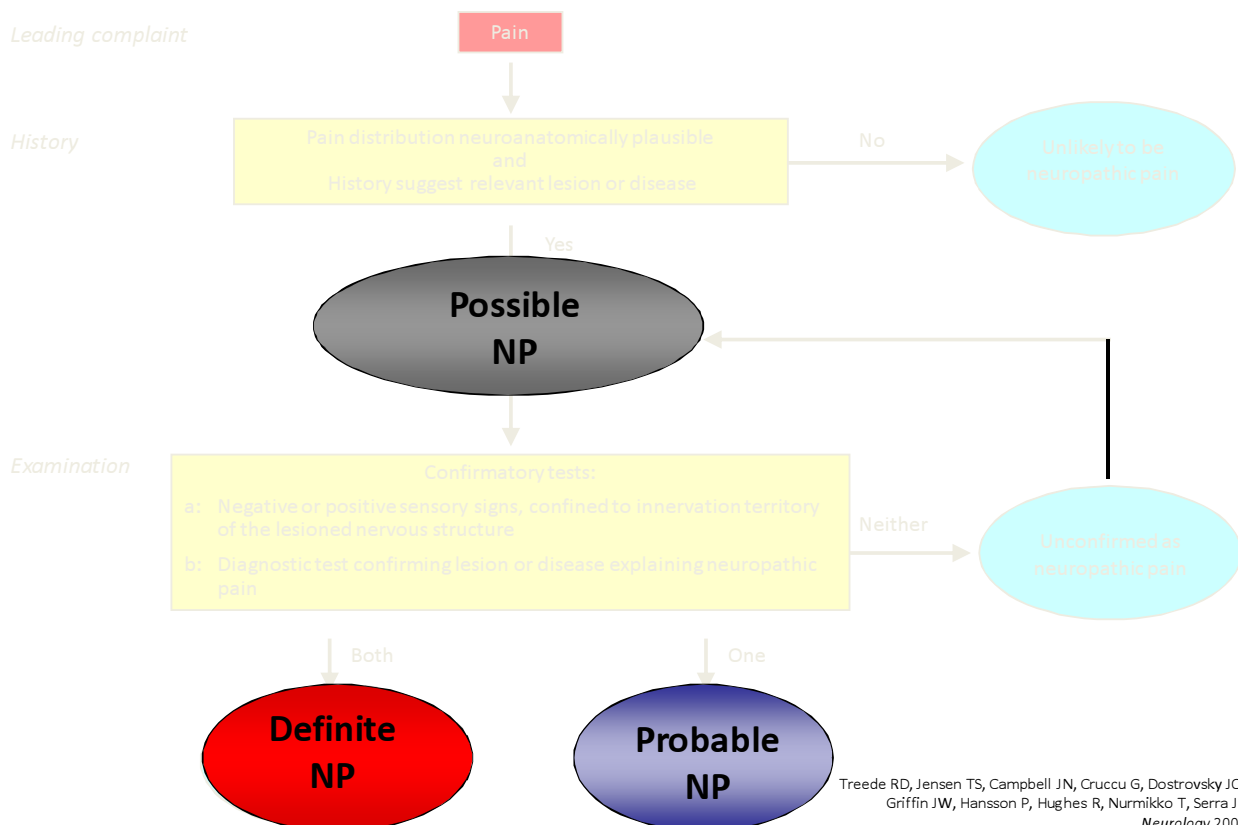
PGP 9.5 non-specific panaxonal marker
 Antibodies against microtubules
 Antibodies against neurofilaments
 Antibodies against myelin
 Immunostaining against TRPV1, VIP, CGRP, SP



Staining for PGP 9.5
 A: Normal
 B: Diabetic neuropathy

Sommer & Lauria, 2007.

Neuropathic Pain: New grading proposal



Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J. *Neurology* 2008

Painful Polyneuropathies

- **Metabolic**
 - Vitamin deficiency
 - Diabetic
 - Insulinoma
 - Malnutrition
- **Drugs**
 - Antiretrovirals
 - Antineoplastic
 - Nitrofurantoin
 - Thalidomide
 - Disulfiram
- **Toxins**
 - Alcohol
 - Acrylamide
 - Arsenic
 - Thallium
- **Hereditary**
 - Amyloid
 - Fabry
 - HSAN type I
 - Tangier
- **Malignant**
 - Dysglobulinemia
 - Direct infiltration
 - Paraneoplastic
- **Infectious/Postinfectious**
 - Vasculitis
 - Zoster
 - Lepra
 - HIV
 - Guillain-Barre
- **Others**
 - Erythromelalgia
 - Idiopathic small fibre neuropathy
 - Cold injury

Modified from Scadding, 2006
Handbook of Neurology

Investigations in painful peripheral neuropathy

- **Blood**
 - Full Blood count
 - SR
 - Renal function
 - Liver function
 - Ca⁺⁺
 - Glucose
 - Fasting lipids lipoproteins
 - B12 Auto antibodies
 - Anti neuronal antibodies
 - Cryoglobulins
 - HIV serology
- **Urine**
 - Urinalysis
 - Bence Jones protein
 - Porphyrines
- **CSF**
- **X-Ray of thorax**
- **Electrodiagnostics**
 - NCS/ EMG
 - QST
 - (Sympathetic skin response)
 - Autonomic function
- **Histopathology**
 - Nerve biopsy
 - Muscle biopsy
 - Skin biopsy

Modified from Ginsberg 2006
Handbook of Clin Neurology

Diabetes and neuropathy: Prevalence

Diabetes

2000: 2.8%

2030: 4.4% (366 mil individuals)

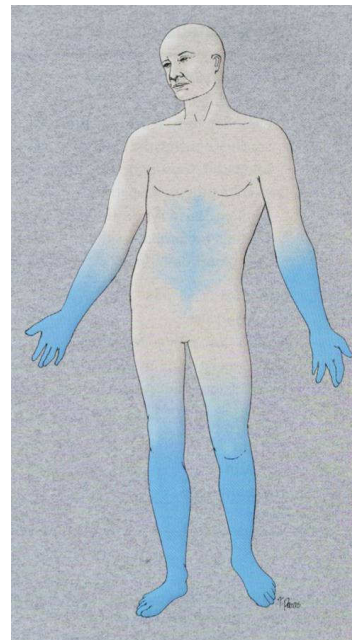
(Wild et al. 2004)

Diabetes and Neuropathy

Male: 71 % clinical neuropathy after 12 yrs

Female: 51% clinical neuropathy 12 yrs

(United Kingdom Prospective Diabetes Study, 1998)



Diabetic Neuropathy: Classification

Rapidly reversible DN

Hyperglycemic neuropathy

Generalized sym. polyneuropathy

Acute sensory

Chronic sensory-motor

Autonomic

Focal and multifocal neuropathy

Cranial

Isolated peripheral (limb)

Mononeuritis multiplex

Truncal (thoracolumbar)

Proximal motor (amyotrophy)

Superimposed CIDP

Chronic sensory-motor

- “Dying back” or “length-dependent” (LD) process
 - Longest nerves affected first
 - End of nerve fibres preferentially affected
 - Time course: months to years
 - Gradual, symmetric
 - Symptoms: predominantly sensory

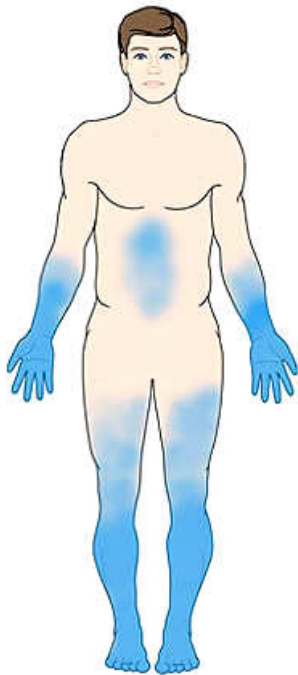
Painful Diabetic Neuropathy : Classification and symptoms

- **Painful Diabetic neuropathy**
 - **Focal and multifocal**
 - Cranial e.g N.III mono NP
 - Focal limb NP e.g. entrapment NP
 - Amyotrophy (proximal motor)
 - Truncal radiculoNP
 - **Generalized symmetric PN**
 - Acute sensory (always painful)
 - Chronic sensorimotor
- **Symptoms and signs**
 - Paresthesia, Numbness dysesthesia/allodynia in feet/hands
 - Paroxysmal, shooting pain
 - Deep aching pain, muscle pain, cramping
 - Allodynia and hyperpathia
 - Autonomic dysfunctions (associated)

Symptoms in PDN: Related to fibre types ?

	Large Fibre Neuropathy	Small Fibre Neuropathy
Symptom	Numbness, P&N Tingling Poor balance	Pain: Burning, electric shocks Stabbing pain
Exam	Reflexes, proprioception vibration	Thermal, pin-prick sensation
Function	Pressure, balance, muscle strength	Pain sensation, protective sensation
Diagnostic Test	NCV testing Sural nerve biopsy	Historically "invisible" QST Nerve biopsy, skin biopsy

Small Fibre Neuropathy SFN



Complaints

- Deep aching pain
- Burning feet
- Pricking sticking sensations

Examination

- Reduced thermal and pain sensation
- Loss of vibration distally in toes but normal at ankles
- Standard nerve conduction studies normal

Delineation

- A subtype of sensory neuropathies predominantly affecting C and A δ nerve fibres

Herpes zoster and PHN



1st pain case

Middle aged male
Severe accident at workplace
Several surgical reconstructions

Complaints:

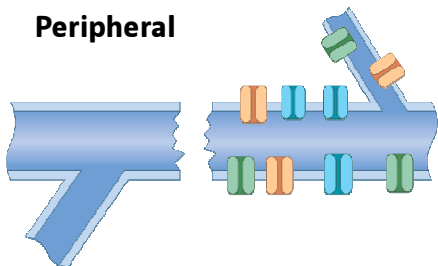
I have pain
I wake up with cramps
I feel miserable.
I can't use my hand
I can't work,
My family has left me



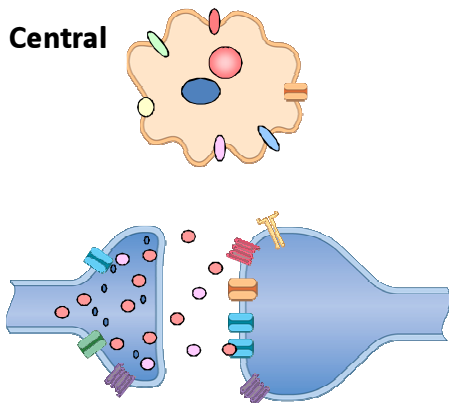
Pain case:

Objective measures

Peripheral

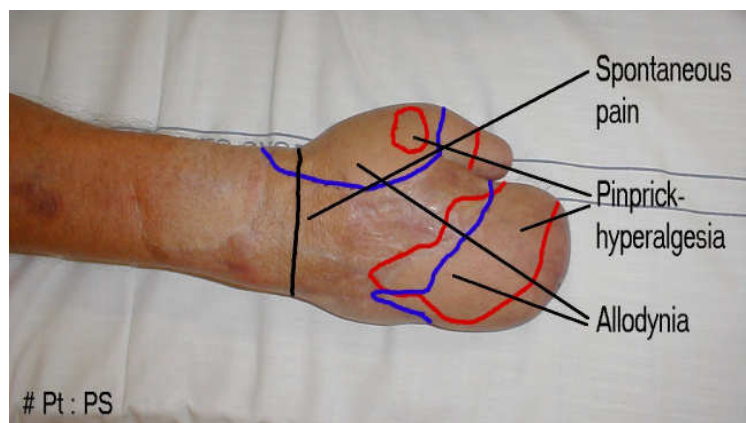


Central

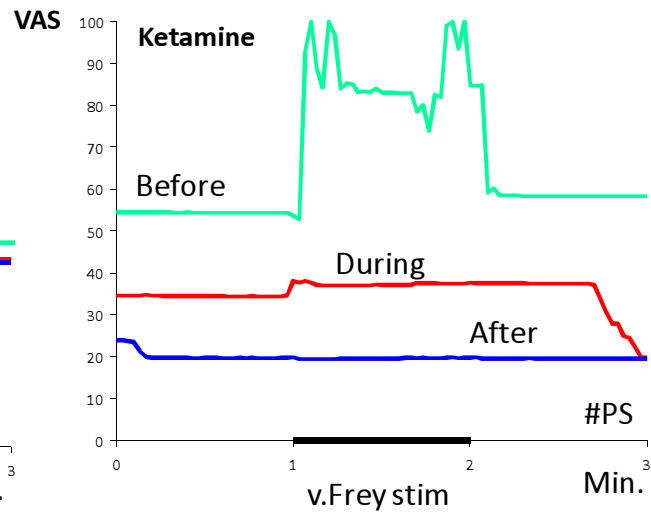
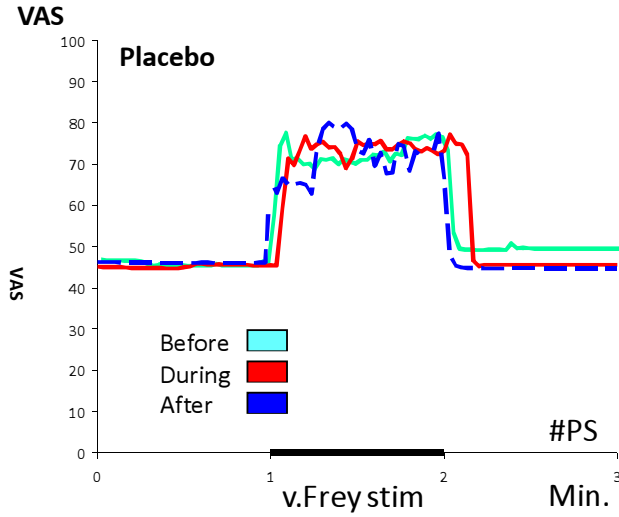
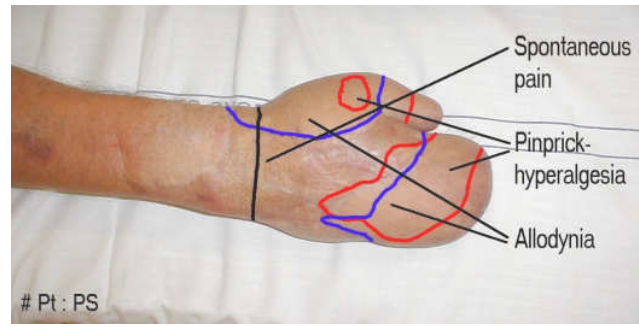


Signs

sensory loss
Hyperalgesia
Allodynia
Target mechanisms



Neuropathic pain:
Modulation of spontaneous and evoked pain



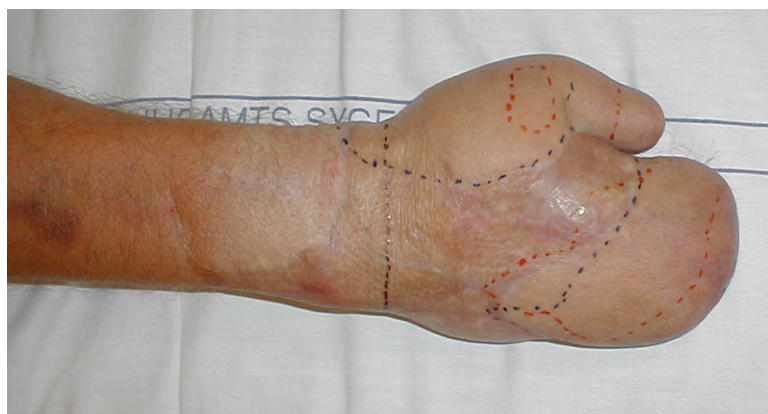
VAS rep. v.Frey 2Hz 1 min.

Management

- Antidepressants, NMDA antag., Anticonv.
- Physical therapy
- Social support
- Psychological support

Complaints:

- I have pain
- I wake up with cramps
- I feel miserable.
- I can't use my hand
- I can't work,
- My family has left me



3rd pain case

- 52 yr old woman mastectomised 4 yrs. ago because of ductal carcinoma
- Glands removed from the axilla followed by radiotherapy
- Has had pain and sensory loss in the right arm since operation
- Complains of swelling of the right arm
- Within the last 6 months increasing pains in the arm and in the spine
- A discrete limping of the right leg has been noted

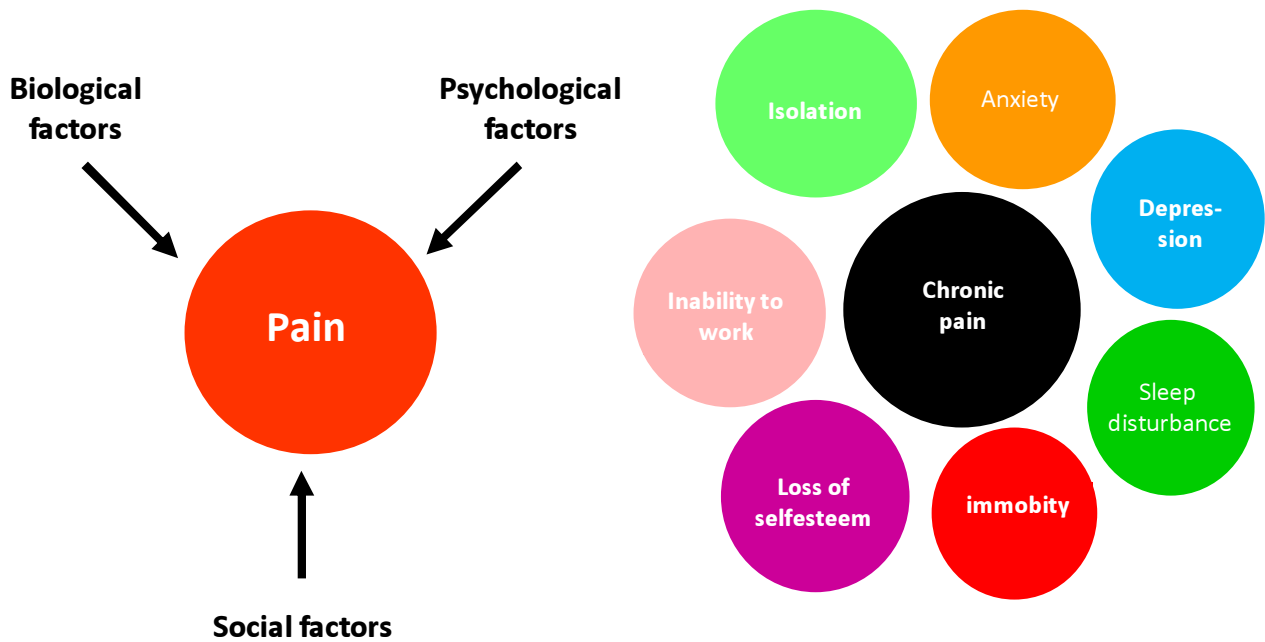
Diagnosis ?

Treatment ?

Causes of Pain: Cancer

- **Cancer-related**
 - Bone
 - Nerve compression/ infiltration
 - Soft tissue infiltration
 - Visceral
 - Muscle spasm
 - Lymphoedema
 - Raised intracranial pressure
 - Spinal cord compression
- **Treatment related**
 - Surgery: postoperative scars /adhesions
 - Radiotherapy: burns/ fibrosis
 - Chemotherapy: neuropathy
- **Associated with cancer/ debility**
 - Constipation
 - Pressure sores
 - Bladder spasms
 - Stiff joints
 - Post-herpetic neuralgia
- **Unrelated to cancer**
 - Arthritis
 - Angina
 - Trauma
 - Prior pain conditions

Comorbidities and problems in chronic pain



Symptoms and signs in chronic pain categories

Pain		Neuropathic	Nociceptive	Mixed
Positive symptoms and signs	Signs of inflammation	no	sometimes	sometimes
	Neuroanatomical distribution	yes	no	variable
	Hypersensitivity	yes	yes	yes
	cold allodynia	often	rarely	?
	Hyperpathia	sometimes	never	sometimes
	aftersensations	often	Rarely	?
	Specific	Paroxysms ?	throb pain ?	none
Negative symptoms and signs	Red. sensation in painful area	often	no	sometimes
	Sensory loss neurol area	yes	no	sometimes
	Motor deficit	Often	no	sometimes