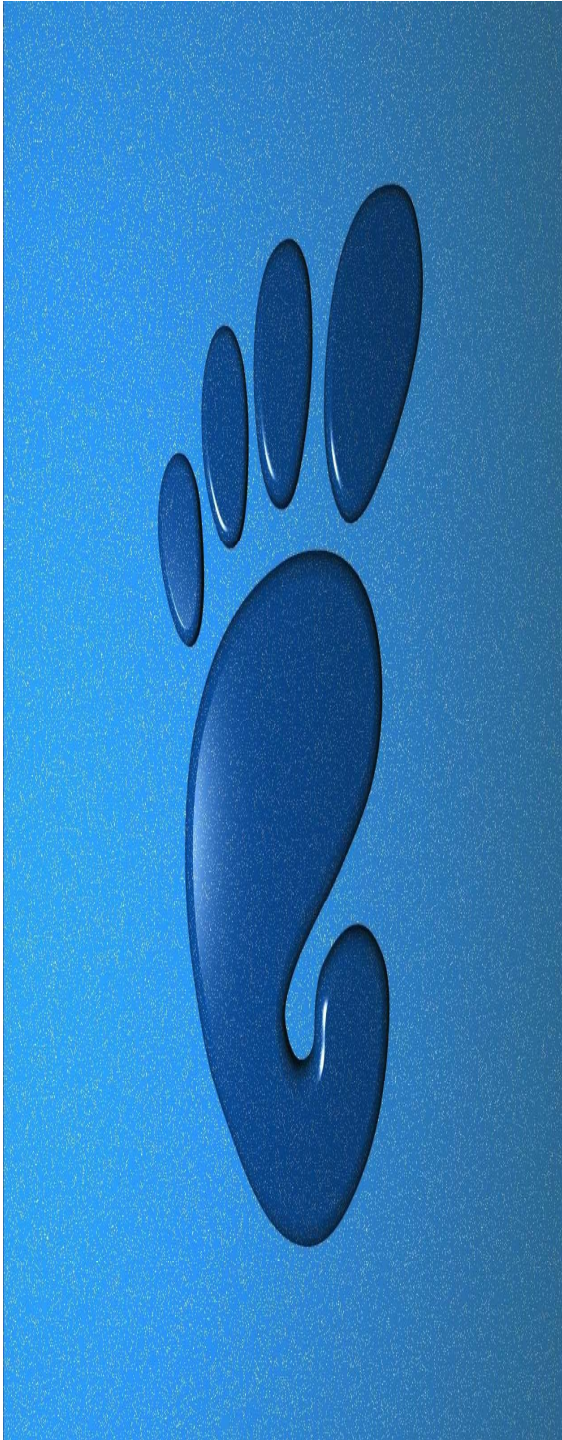




Diabetic Neuropathy The Pathway To Ulceration

Manal Farshoby
Diabetic Foot Team
Mansoura University

DF workshop 25/1/2007



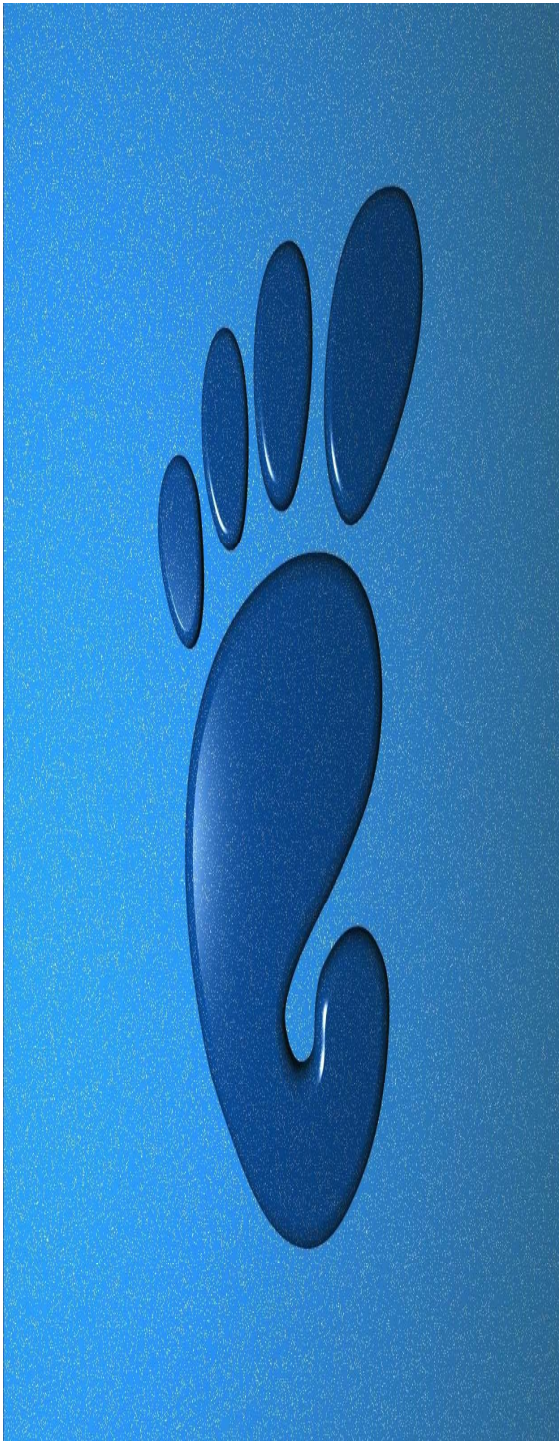
A Problem ! ! !

- Affect every tissue
- Significant morbidity
- Neuropathy related to 50-75% of non traumatic amputation.

A Problem ! ! !

- Physicians miss the diagnosis of DPN in 61% of patients.
- Severe neuropathy goes undetected in about one-third of cases.

Diabetes care 2005



A Problem ! ! !

- 7% of diabetics have neuropathy at diagnosis
- 50% after 25 years.
- Impossible true prevalence.
- Variable criteria of diagnosis.
 - symptoms, signs, tuning fork, monofilament or nerve conduction studies.

What is Diabetic Neuropathy?

The presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes.

(International Consensus Meeting, 1993).



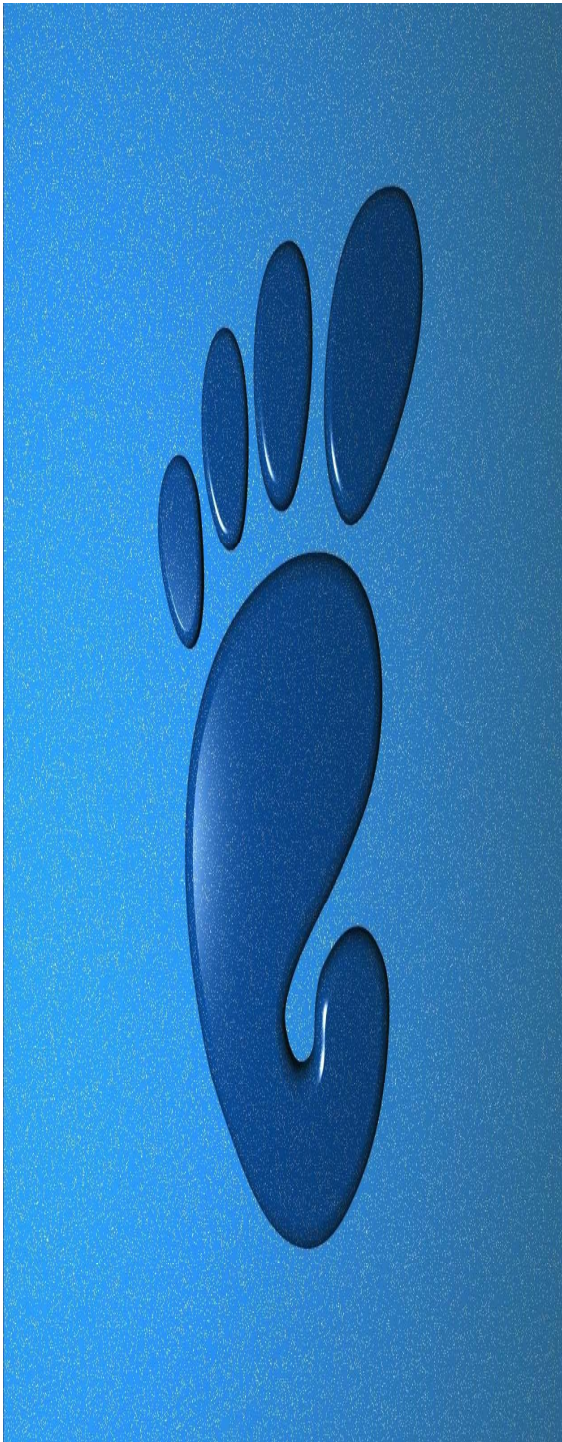
IS IT DPN ?

- The patient is diabetic.
National Diabetes Data Group criteria.
- Prolonged chronic hyperglycemia.
- Predominant distal sensorimotor polyneuropathy in the **lower extremities**.
- Associated diabetic retinopathy or nephropathy.
- **Exclude other causes**



10%

- Toxic:
 - Endogenous (uremia, liver disease)
 - Exogenous (arsenic, lead, mercury)
- Drugs : Hydralazine INH , nitrofurantoin, vincristine and Chloroquine
- Endocrinal:
 - Hypothyroidism, Acromegaly.
- Nutritional, Vascular, Sarcoidosis, Malignancy, Acute inflammatory polyradiculoneuropathies.
- Leprosy



Pathogenesis

- **Hyperglycemia**
- **Other mechanisms**
 - Polyol pathway
 - ↓ Myoinositol
 - Oxidative stress
 - Glycation
 - Vascular factors
 - Growth factors
 - VEGF
 - Insulin-like growth factors
 - Immune mechanisms
 - C-peptide

Diabetic Neuropathy



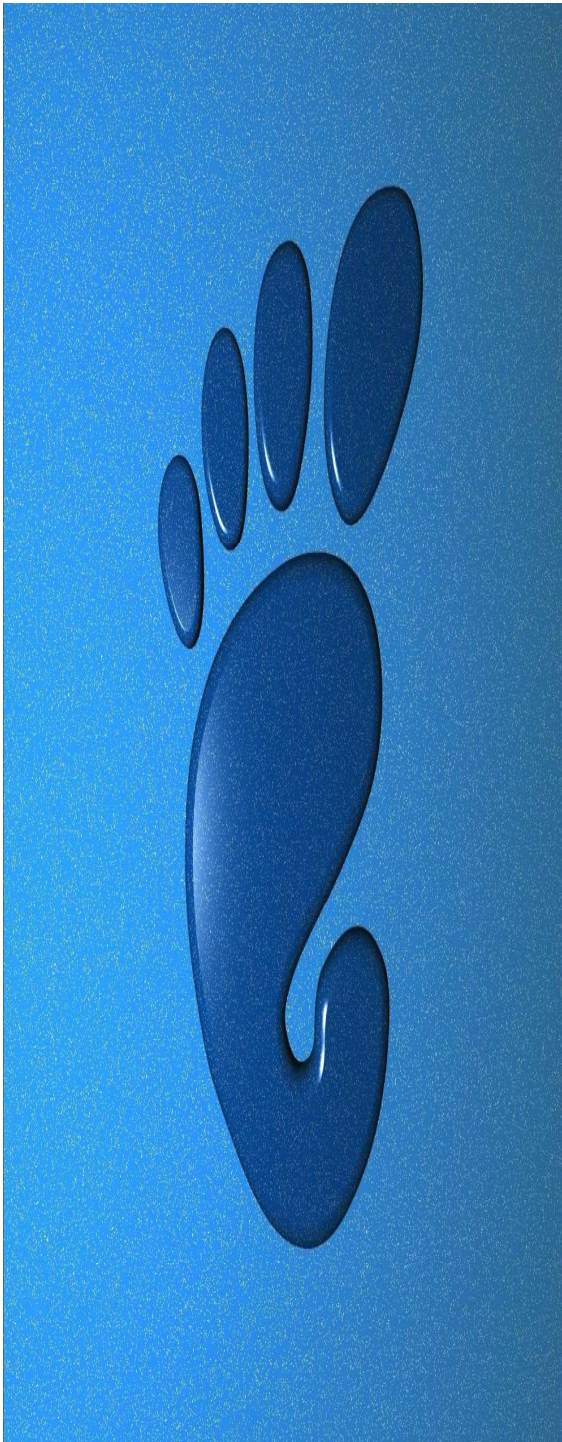
**Symmetrical
polyneuropathies**

- **sensory**
- **motor**
- **autonomic**

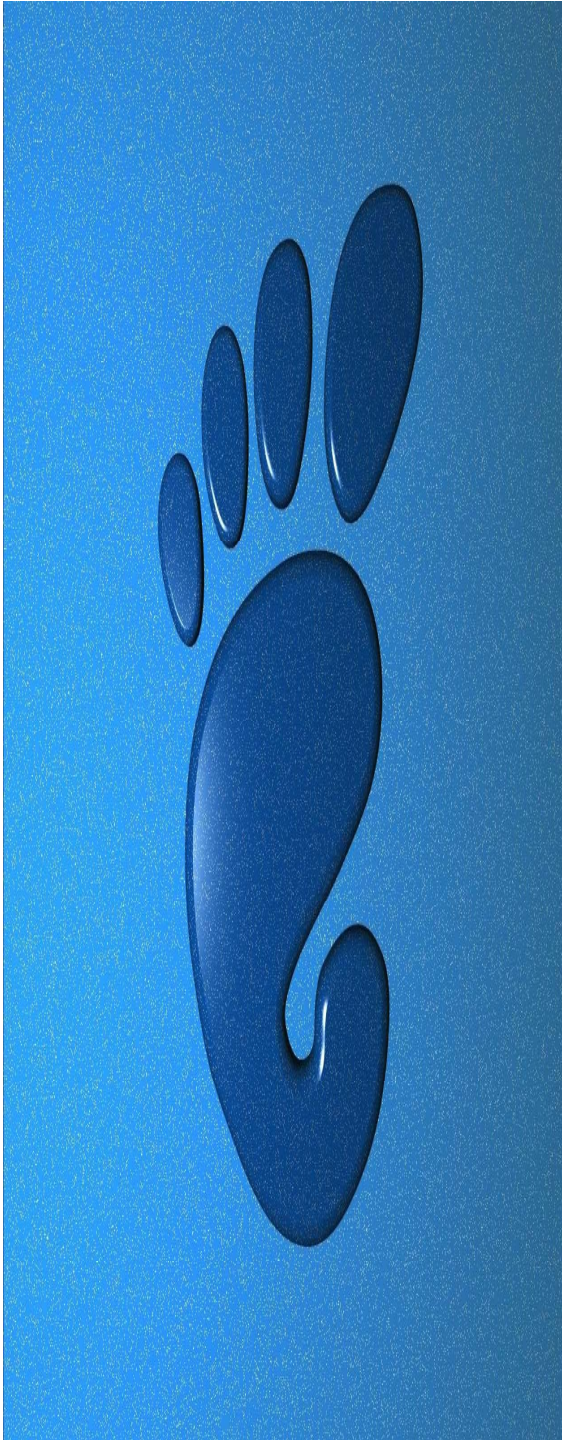
Focal neuropathies

- **Mononeuropathy**
- **mononeuropathy
multiplex**
- **plexopathy**
- **Radiculopathy**
- **cranial neuropathy**

Paradox ?



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**Pain is God's greatest
gift to mankind**

Paul Brand

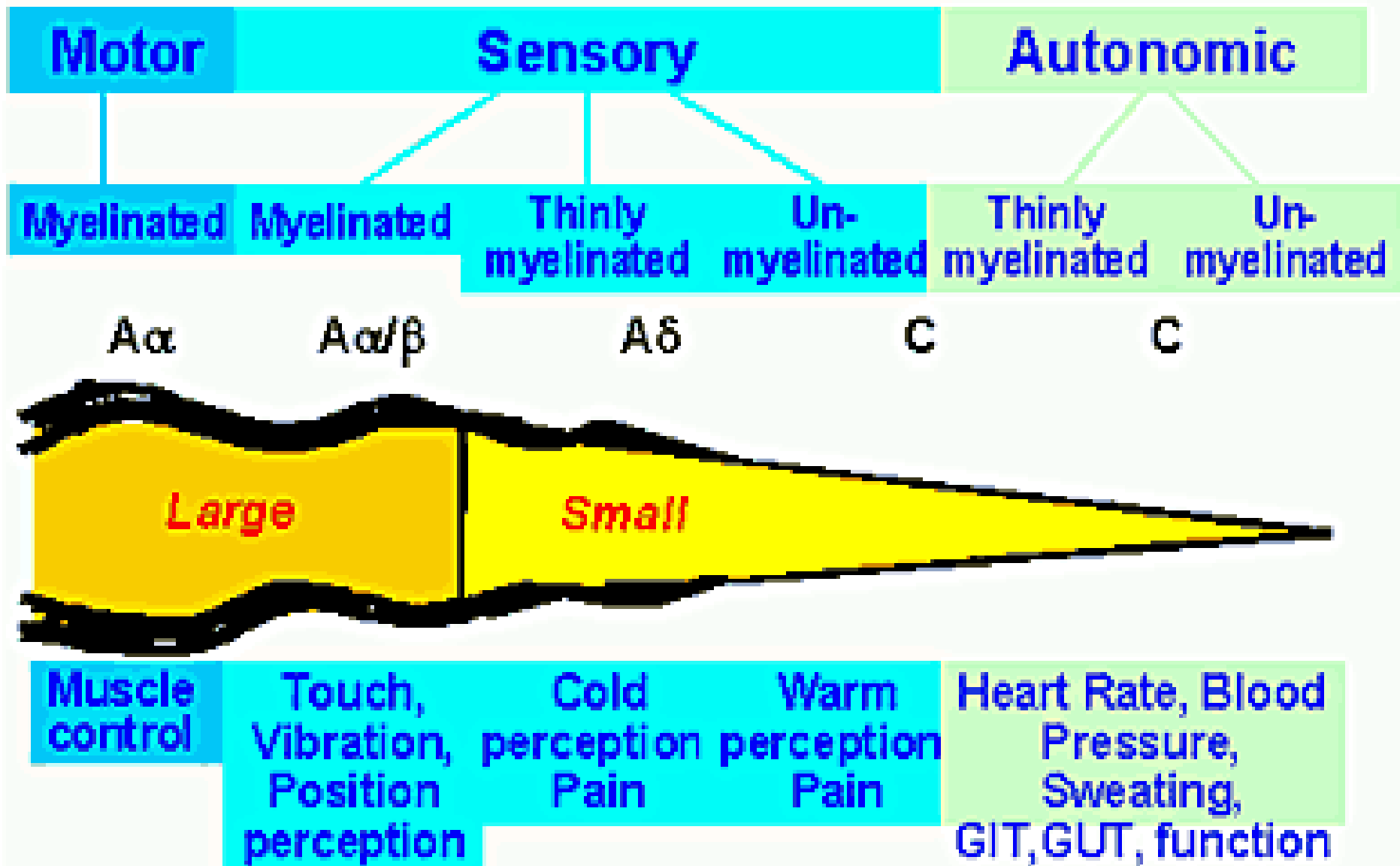
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Painful-Painless Leg

- One doesn't need to have intact sensation to experience pain.



A Simplified View of The PNS



Distal Symmetric Diabetic Neuropathies

➤ Large fiber



➤ Small fiber



Complaining ! ! !

➤ Pain

- Burning.
- Throbbing.
- Freezing.
- Lancing
- Like a nettle sting.
- Freezing.
- Shooting.
- Shock-like.
- Knife-like.
- Allodynia
- Hyperalgesia



Pain

- peculiar to the individual patient
- constant during the history of neuropathy in that individual.
- More at night
- <20%

Complaining ! ! !

➤ Negative symptoms

- Prickling.
- Tingling
- Feet feel dead

Complaining ! ! !

➤ Unsteadiness

➤ Falls 14x

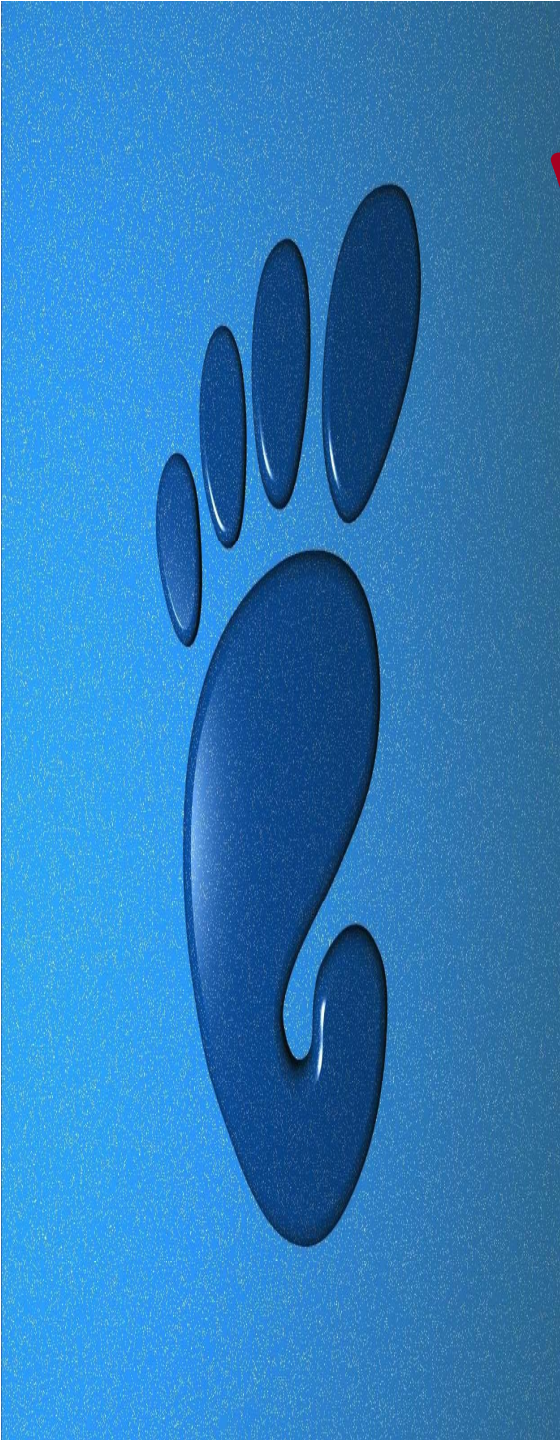
➤ Fractures.



Complaining ! ! !

50%

NO SYMPTOMS

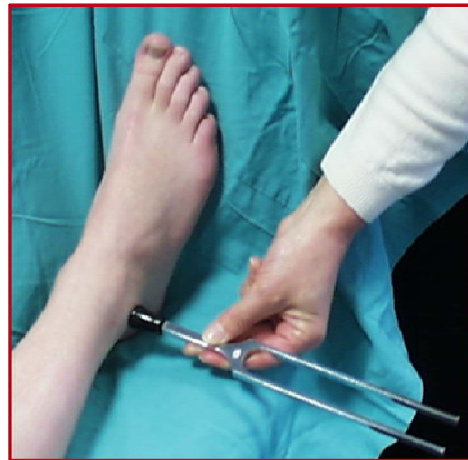
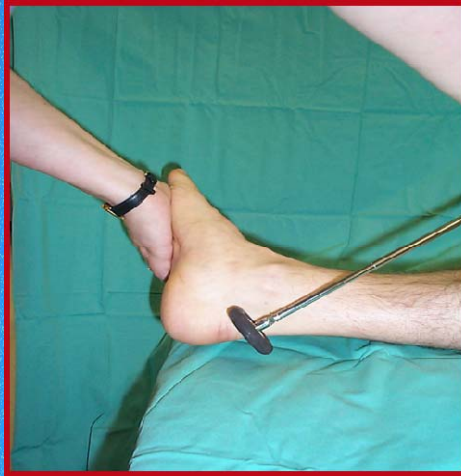


What is your algorithm for management diabetic neuropathy?

- Screening.
- Assessment of severity.
- Glycemic control.
- Patient Education.
- General measures.
- Treatment of pain.

Screening

- ADA screening guidelines



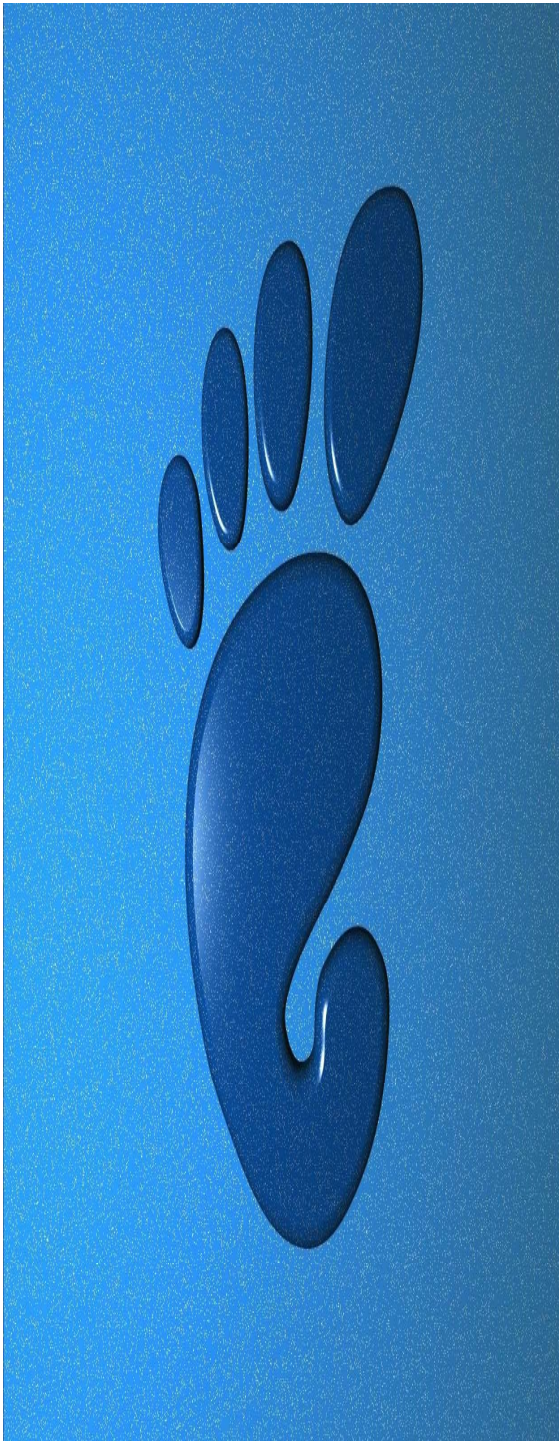
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Screening

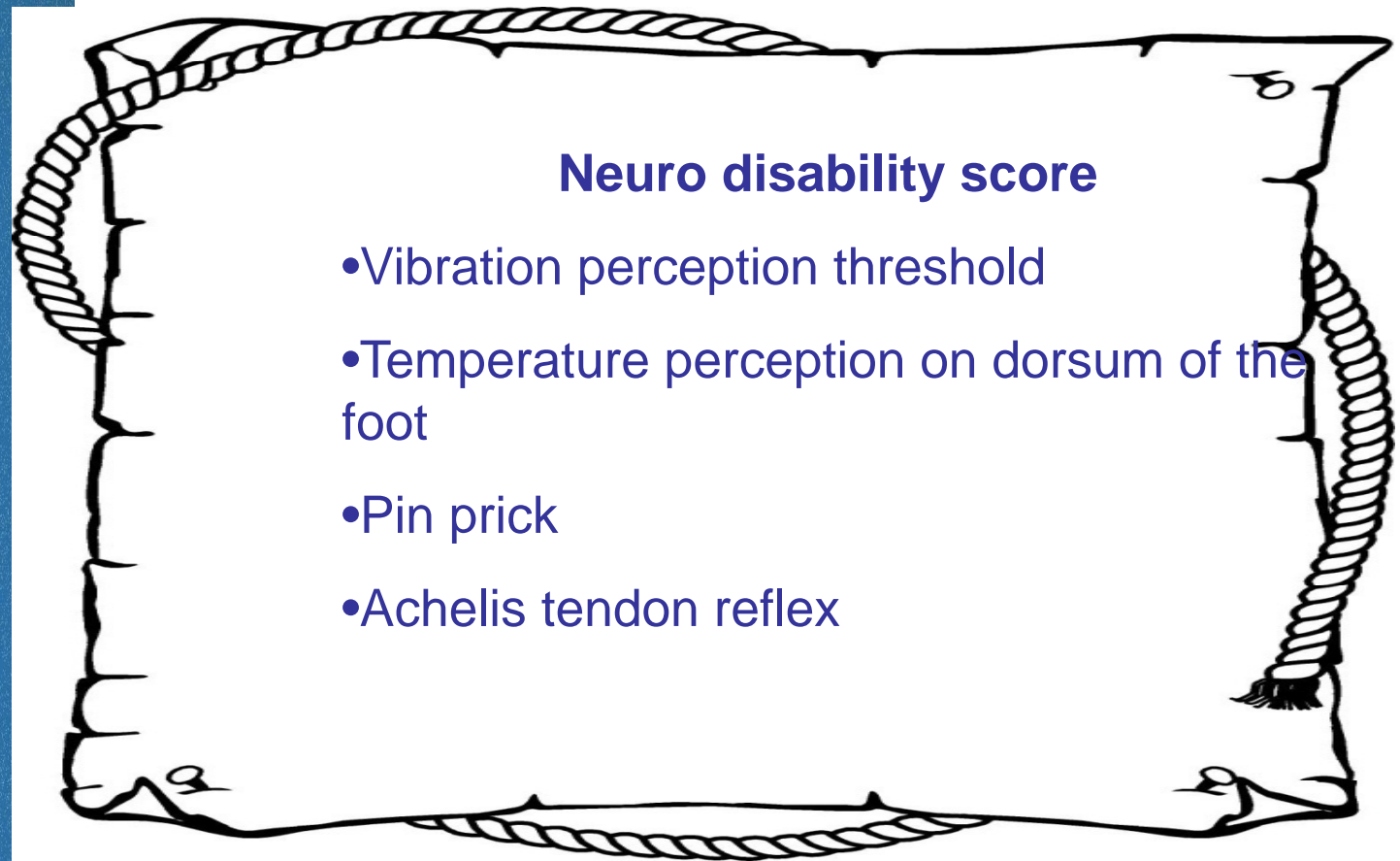
- Simple Bedside Test of Large Fiber Function

Failure to stand on one feet!

Resnick, Vinik et al. *Muscle and Nerve*, 2001



Severity of neuropathy



Neuro disability score

- Vibration perception threshold
- Temperature perception on dorsum of the foot
- Pin prick
- Achelis tendon reflex

Nerve conduction velocity

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Total out of 10

Glycemic control

➤ Prevent DPN

- 63% reduction in DCCT
- ↓ 1% A1C → 1.3 m/s change in nerve conduction velocity over 8 year

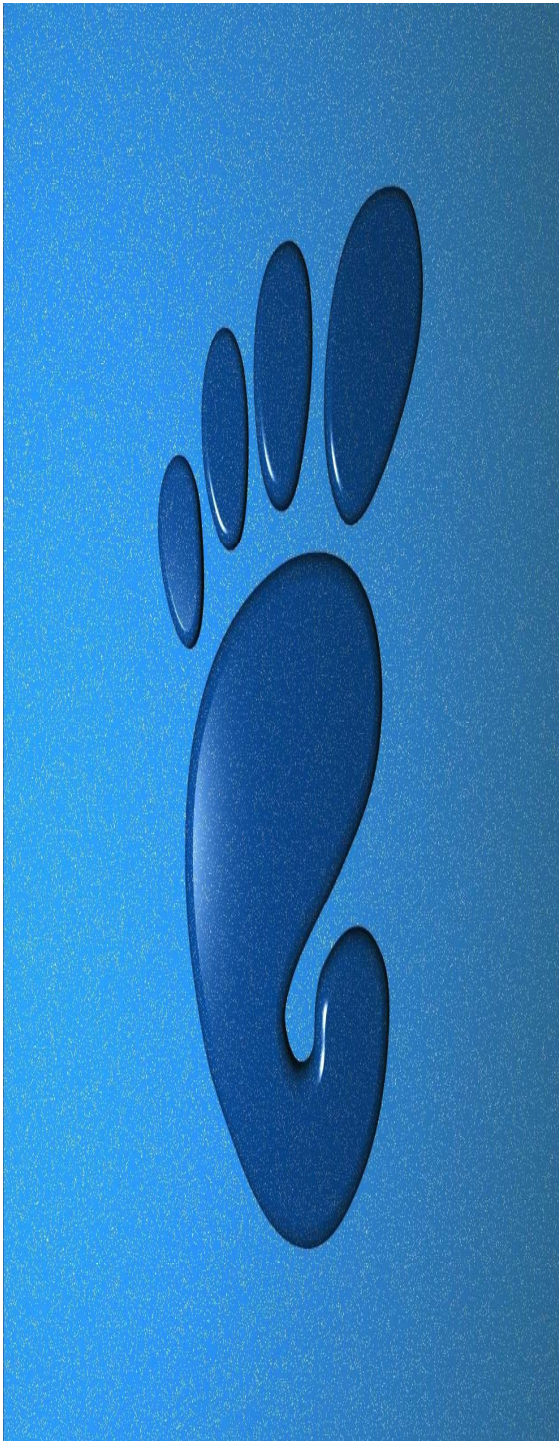
➤ Improved established DPN

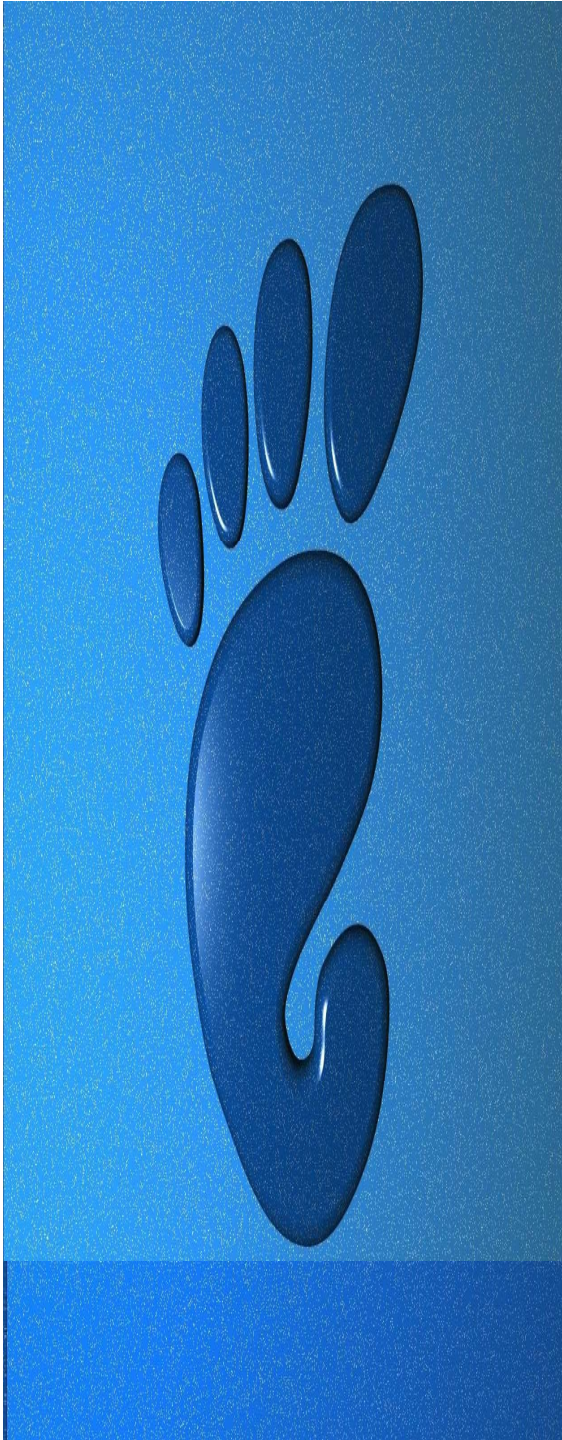
- DCCT
- UKPDS

Glycemic control

Avoid Blood Glucose Fluctuation

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Patient education

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General measures

- Orthotics.
- Muscle strength and coordination training.
- Tendon lengthening.
- Surgical reconstructions.



Treatment of pain



Drug therapy	Non Pharmacological therapy
<ul style="list-style-type: none">➤ Antidepressants➤ Anticonvulsant➤ Antioxidant➤ Opiates➤ Aldose Reductase Inhibitor (ARI)➤ Vasodilators➤ Protein kinase C -B inhibitors➤ Topical Therapy	<ul style="list-style-type: none">➤ Acupuncture➤ Anodyne Therapy System➤ Low intensity Laser therapy➤ Magnetic field Therapy➤ Transcutaneous Electric stimulation➤ Decompression surgery➤ Electric spinal cord stimulation

It's often, 'let's see what works for you.'

- Individualize Drugs
- Combine therapy
- Dose Titration



Antidepressant

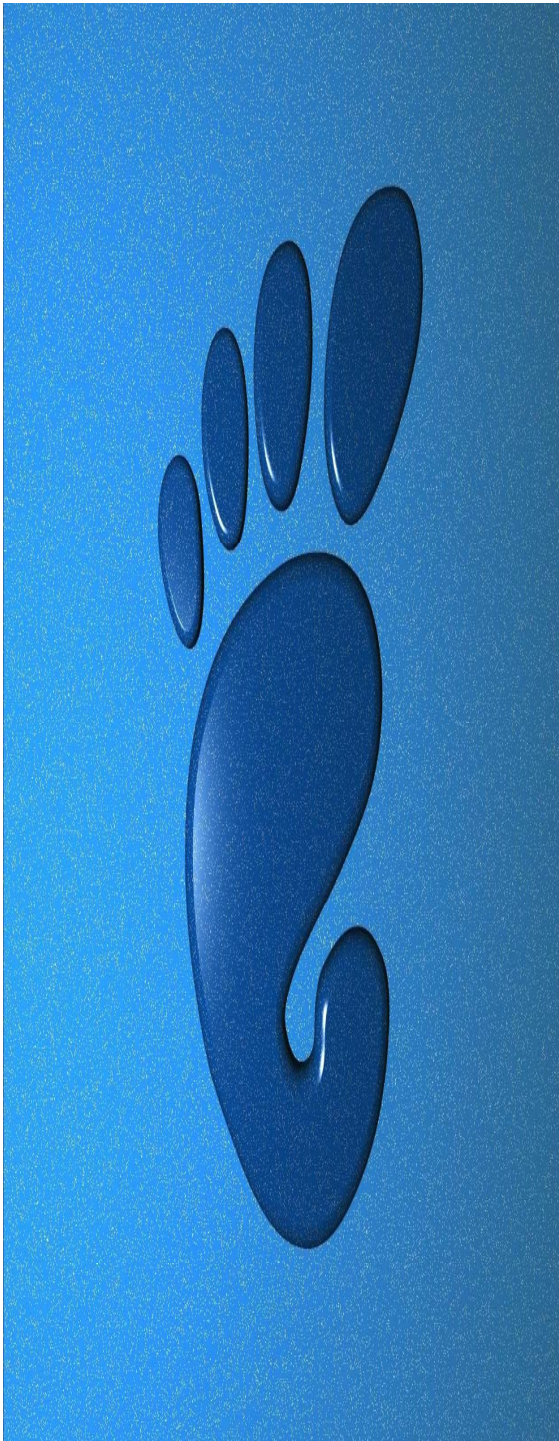
Tricyclic antidepressants:
(Amitriptyline, Imipramine)

- Inexpensive,
- Anticholinergic, fatigue and drowsiness
- Exacerbate some autonomic symptoms such as gastroparesis.

Antidepressant

Duloxetine


- Interacting with serotonin norepinephrine and chemicals believed to play a role in pain.
- FDA approved.



Anticonvulsant

- **Gabapentin** Na channel blocker
 - Start at a small dose and then increase over days to weeks
- **Pregabalin**
- longer acting
- FDA approved
- Reduces the pain of DPN by binding to a protein within "over-excited" nerve cells
- Minimal side effect

Antioxidant

- 
- **Alpha -Lipoic acid (Thioctic acid)**
1200-1800 mg PO QD
IV 600 mg qd for 3 wk
 - Directly regenerate Vitamin C.
 - Indirectly regenerate Vitamin E
 - increase intracellular glutathione.? Retina ? CVD ?
Cerebral i.e Glycosylation!

Antioxidant

➤ Alpha -Lipoic acid

- Correct motor nerve conduction velocity.
- Correct endoneuronal blood flow defect.
- Slow the progression of DPN

Antioxidant

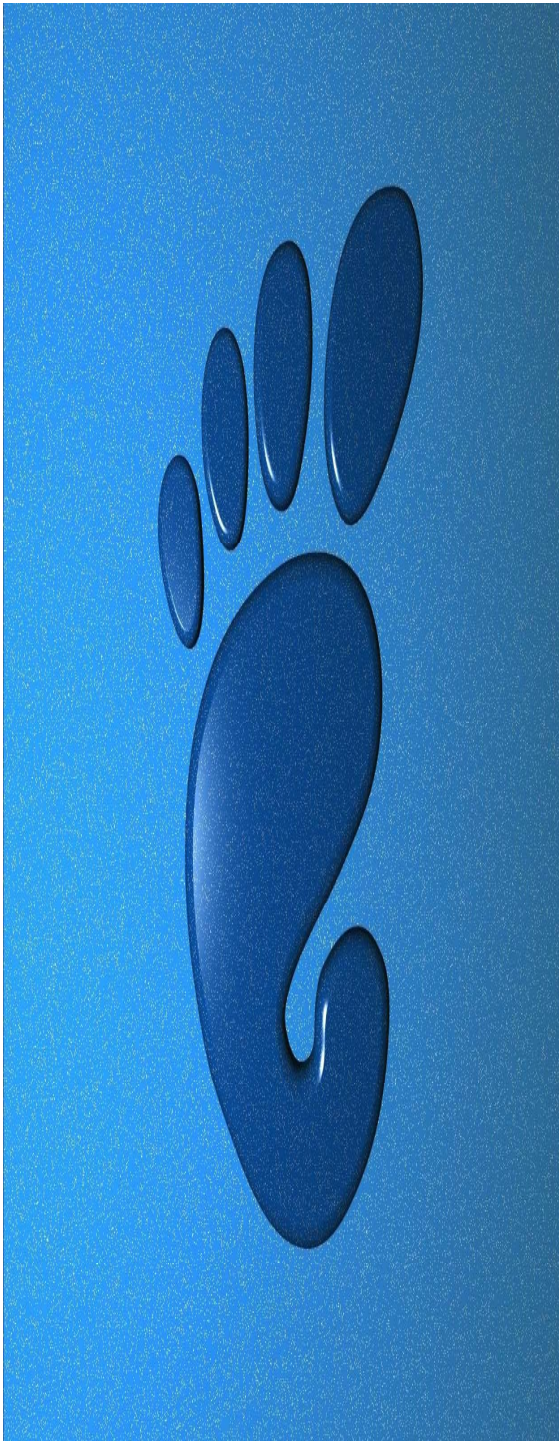
- Benfotiamine
- prevent AGE formation
- Decrease pain
- Restore nerve function
- Retinopathy , nephropathy

Opiates

➤ Tramadol

- low potential for abuse
- controversial.

Analgesic Anti-arrhythmic



Aldose Reductase Inhibitor (ARI)

- Most are withdrawn from the market

Eparlestat

Decrease nerve sorbitol
Marketed in Japan

Vasodilators

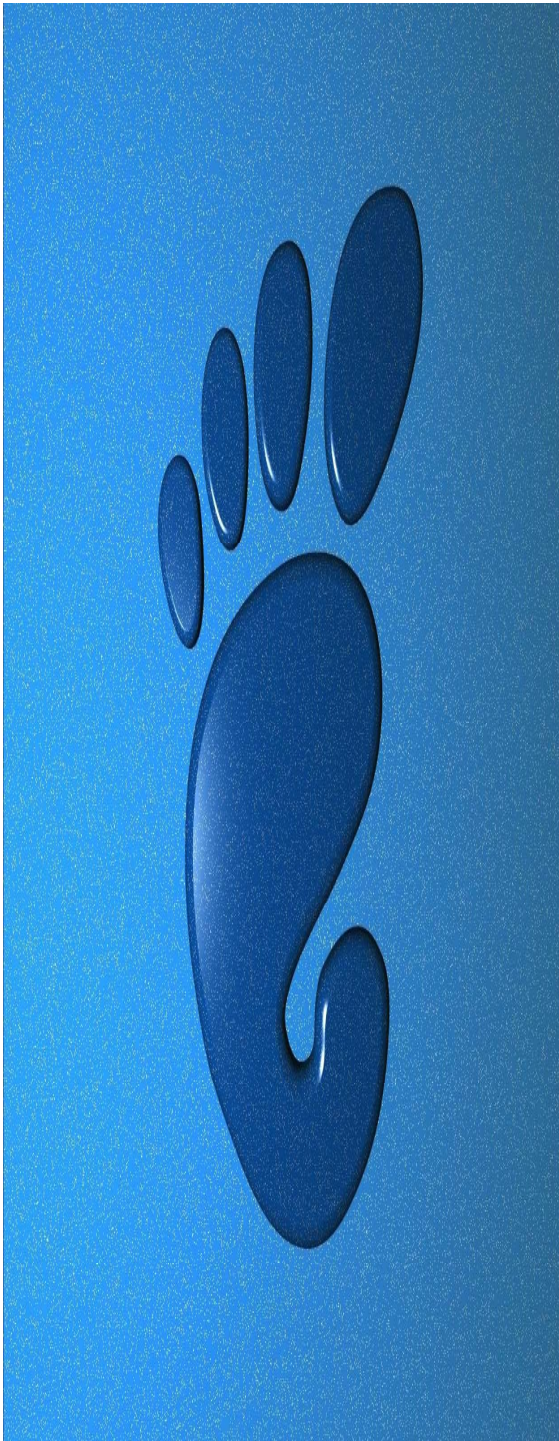
- ACE inhibitors
- Prostaglandin analogue
- NO doners

Increase nerve blood flow

Protein kinase C -B inhibitors.

Promising
Aetiological

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Topical Therapy

- Minimal systemic side effects
- No drug-drug interactions
- Usually no need for drug titration

Topical Therapy

- Isosorbide dinitrate spray or patch
- Topical Capsaisin
 - Depletes tissue of substance P and reduces chemically induced pain
 - Max 8 wks
 - Hyperalgesia
- local anesthetic creams

A blue footprint graphic on a blue background. The footprint is composed of several dark blue, glossy, oval shapes that form the toes and the main body of the foot. The background is a lighter blue with a fine, textured pattern.

Non-Pharmacological Treatment

Acupuncture

- Last for up to 6 months
- Reduce the use of other analgesics

Anodyne Therapy System (Near-infrared phototherapy)

- approved by the
FDA in 1994
- increase
circulation
decrease pain
- improve balance
for some
patients

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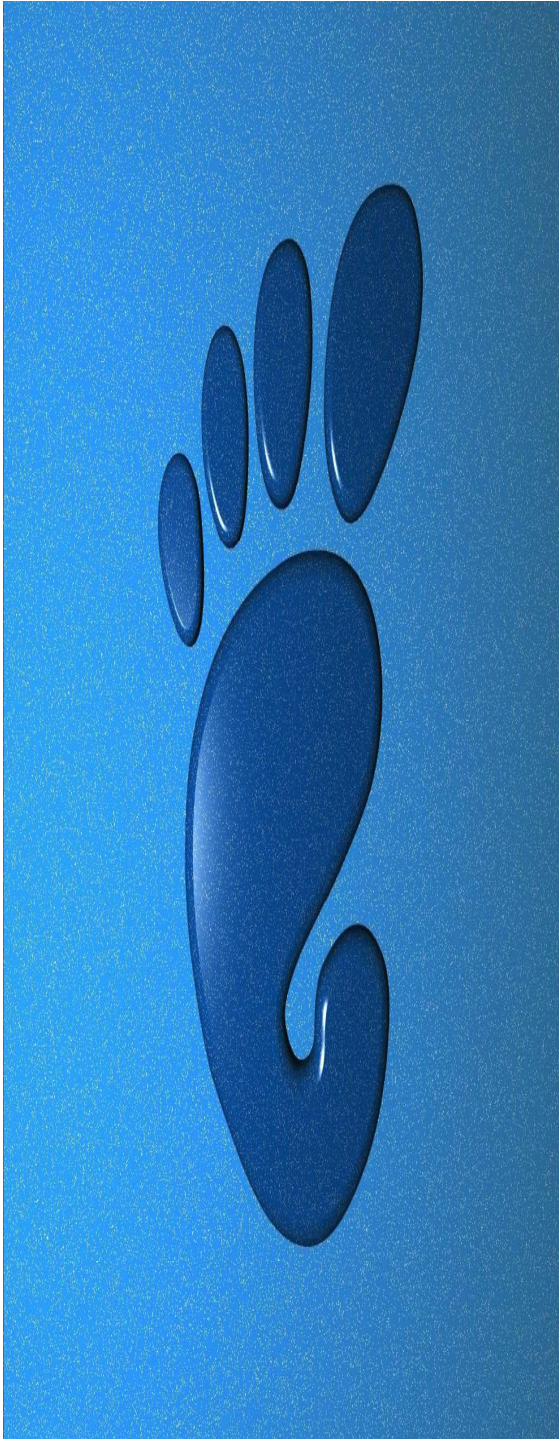
Low intensity
Laser therapy

Magnetic field
Therapy

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Decompression surgery

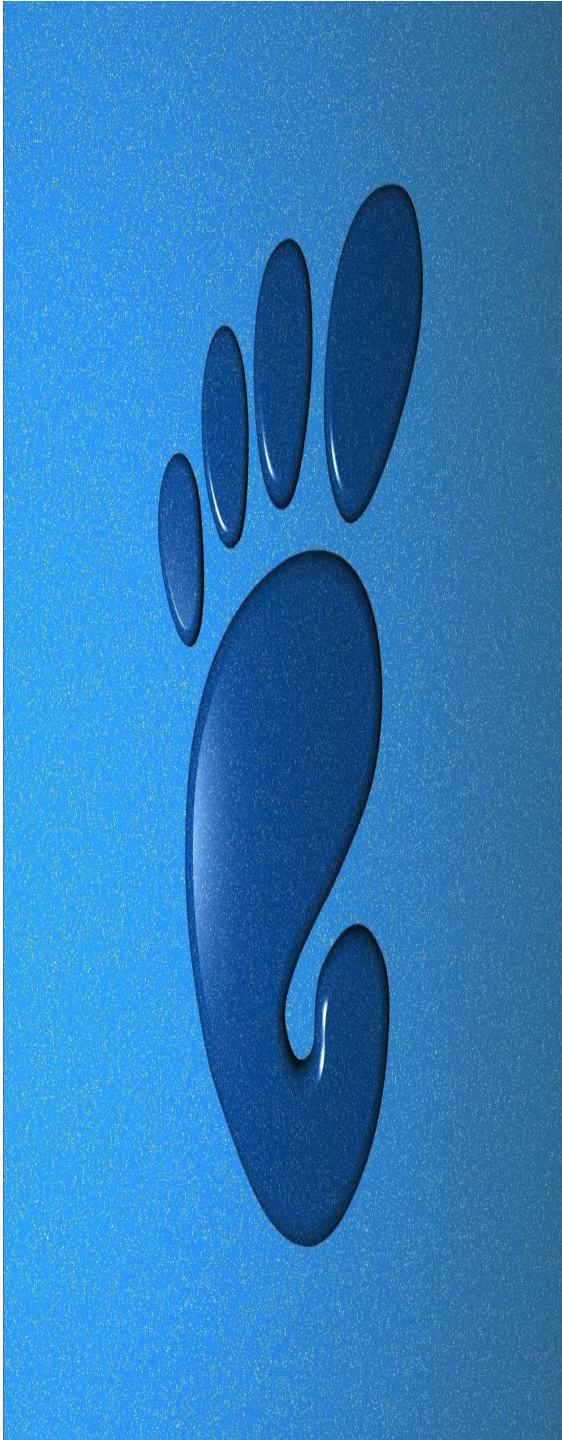
- Decompression of the tibial and peroneal nerves
- Relieves pain and restores sensation in patients with symptomatic diabetic neuropathy
- Only when they're absolutely necessary



- Transcutaneous Electric stimulation
- Electric spinal cord stimulation

Key points

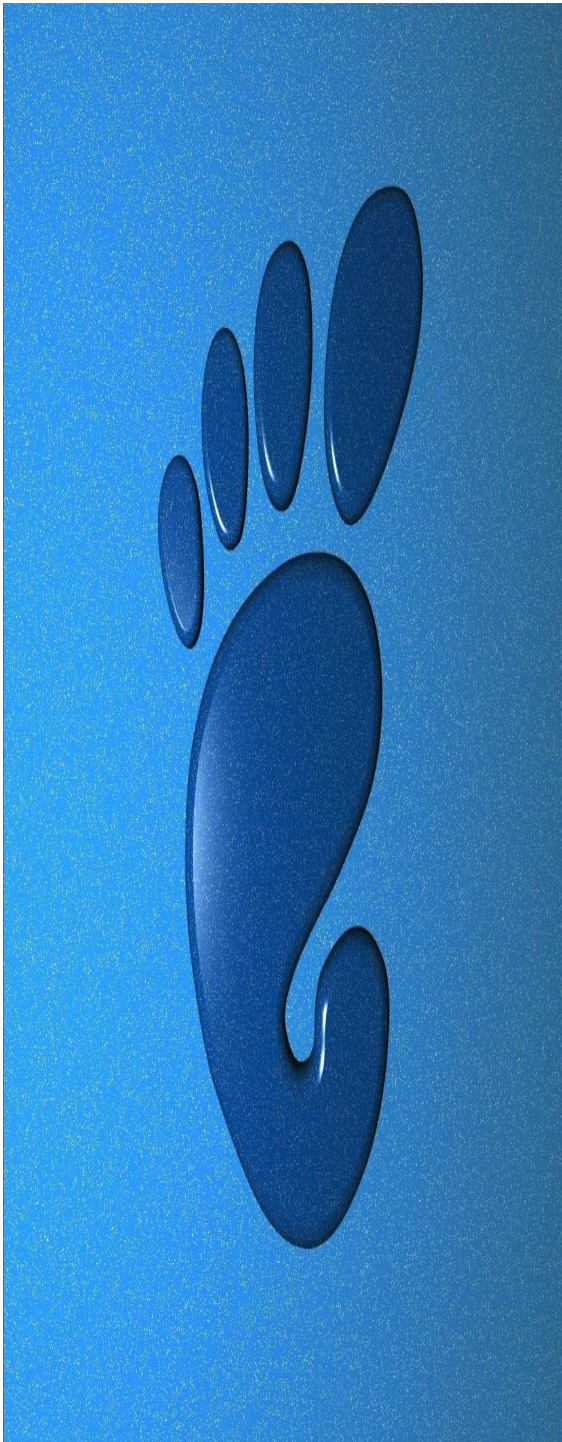
- Informing the patient that pain may resolve in time can be extremely reassuring
- Make sure the patient knows that maintaining consistent glycemic control is critical to managing DPN.
- Drive home the importance of inspecting feet daily and general foot care.



"Success is not final,
failure is not fatal: it is
the courage to continue
that counts."

Winston
Churchill

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THANK YOU



MANAL

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