

# Peripheral Neuropathy – overview and update

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# Faculty/Presenter Disclosure

- **Faculty:** Gary Klein
- **Relationships with commercial interests:**
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  - **Other:** Self employed physician

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## Order an Ankle X-ray if:

- Bone tenderness at A
- Bone tenderness at B
- Inability to bear weight both immediately and in ED

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# Objectives

- Overview of length dependent peripheral neuropathy
- Review of treatment options

# Not included

- Entrapment neuropathies ie CTS
- Traumatic nerve injury
- Acquired demyelinating neuropathy ie GBS
- Inflammatory neuropathy

# And of course – we can't keep it simple

- Peripheral neuropathy
- Distal symmetric polyneuropathy (DSP)
- Length dependent peripheral neuropathy
- Axonal neuropathy

# Basic concept

- This is a disease of the neuron – in this case the cell body situated in the dorsal root ganglion OR the anterior horn cell of the motor system
- The part of the cell body furthest from the nucleus ‘dies back’ first ie the distal axon
- Symptoms begin in the toes and work back from there

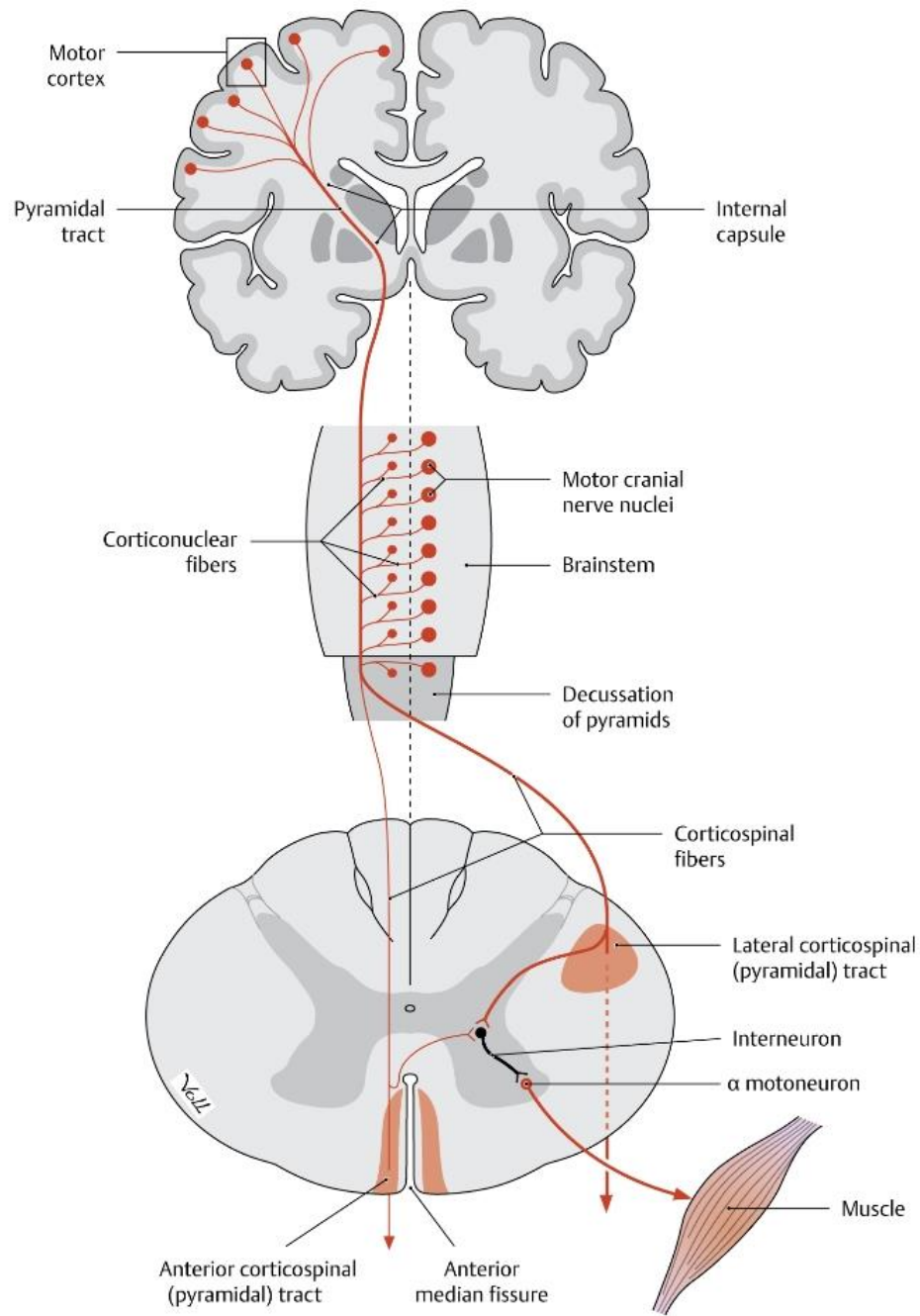


Fig. 6.6  
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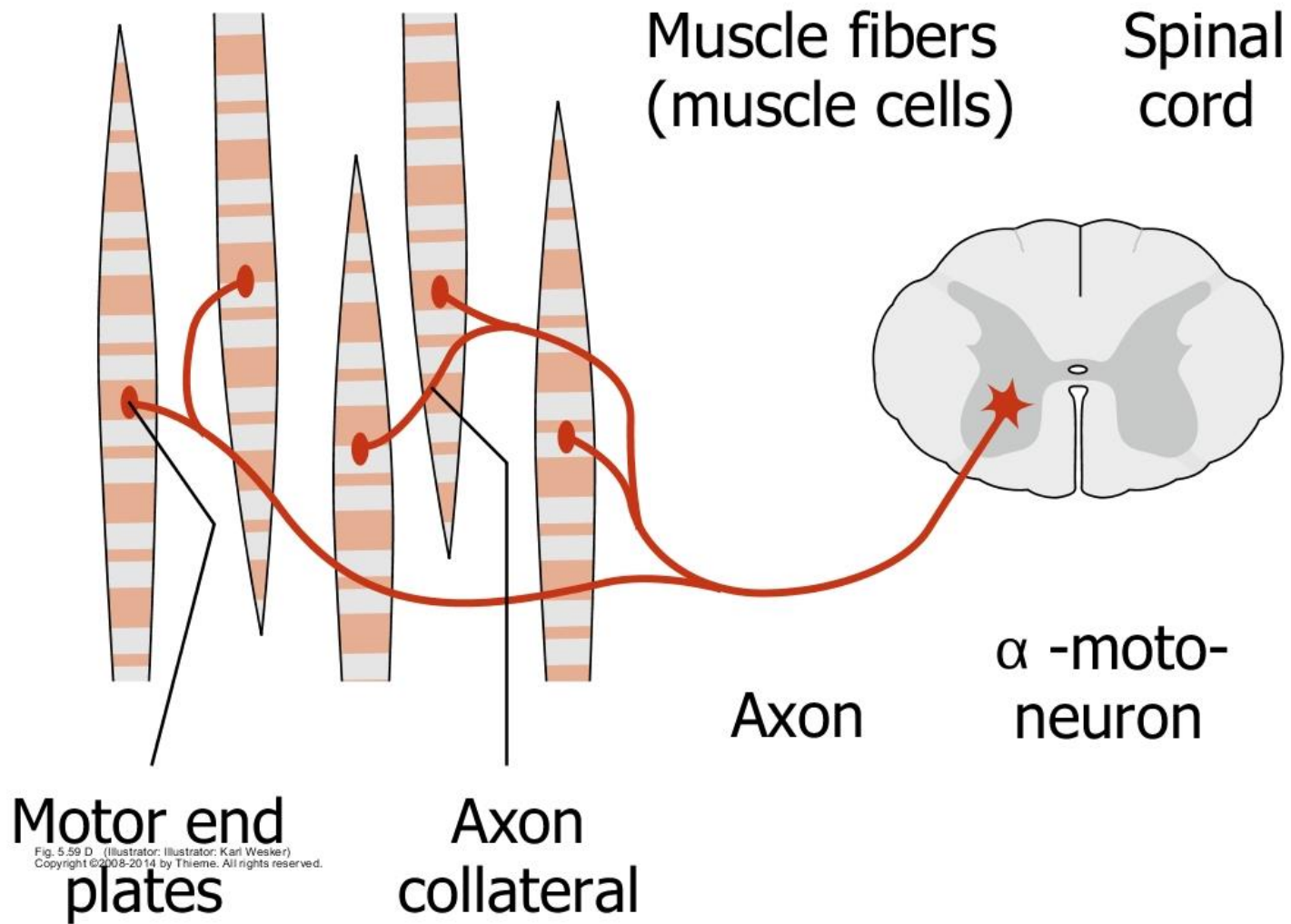


Fig. 5.59 D (Illustrator: Karl Wesker)  
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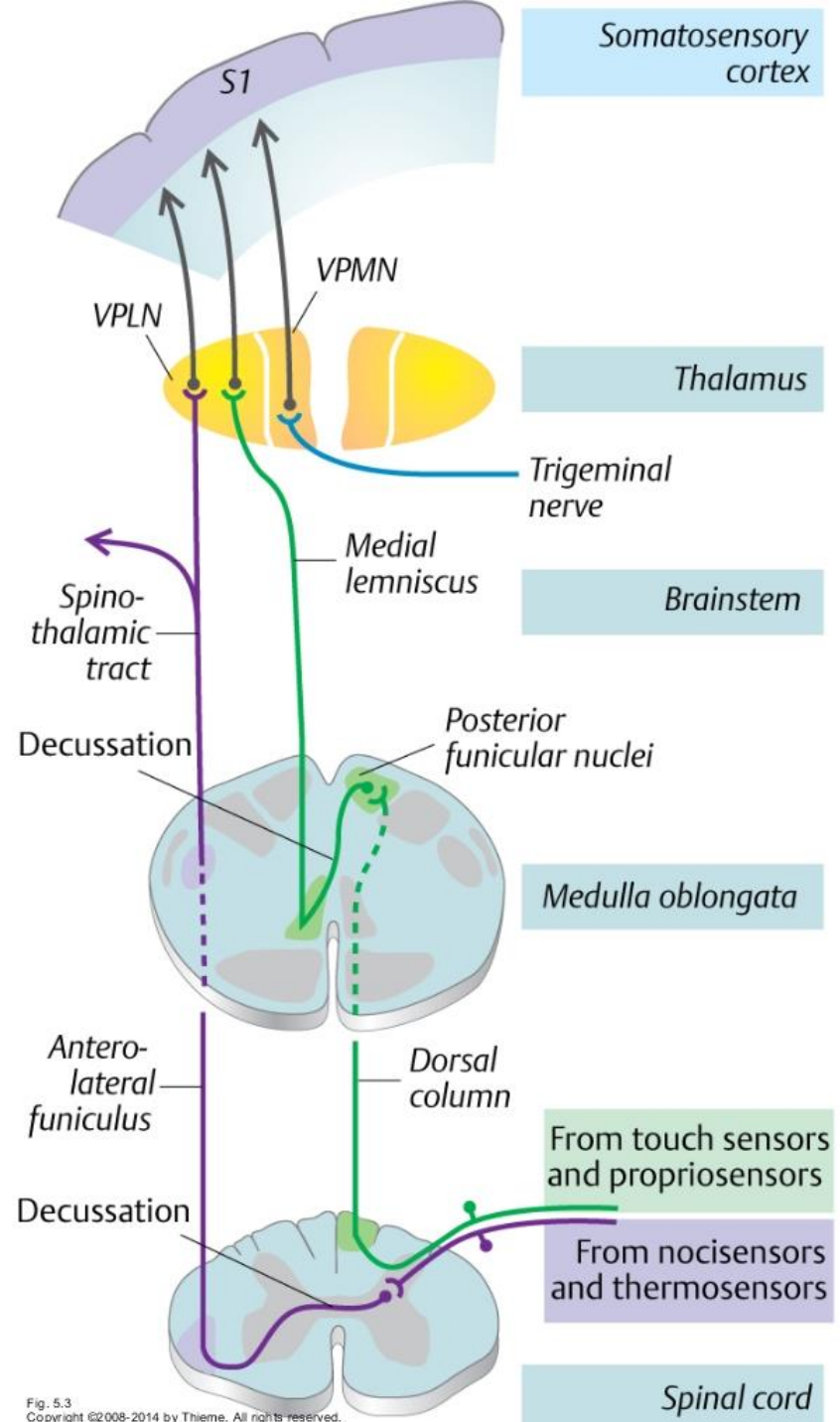
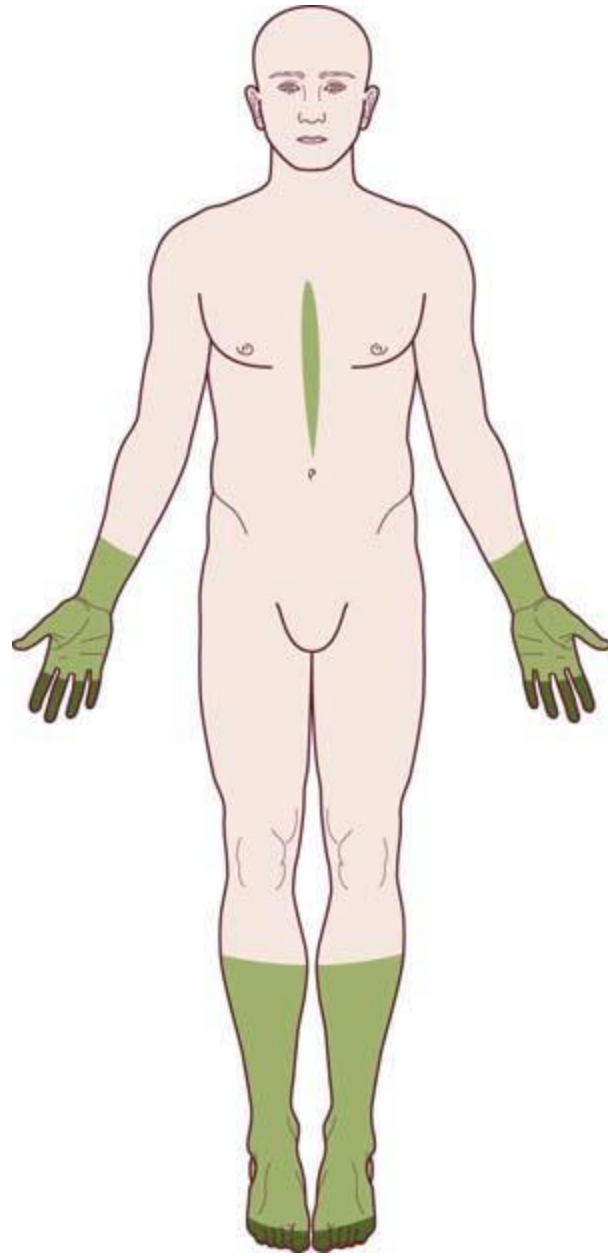


Fig. 5.3  
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- Large sensory fibres - numbness
- Small sensory fibres – numbness, pain, autonomic features
- Motor axons – distal weakness \*LMN syndrome\*
- BUT almost always begins with sensory symptoms

# Lower motor neuron syndrome

- Muscle tone normal or reduced
- Weakness with wasting
- Reflexes reduced or absent
- Absent Babinski response – downgoing toes

- Is this disease common or rare??

# Defining the problem (Callaghan et al 2014)

- Diseases of the of the peripheral nervous system (PNS) account for >10% of all neurologic appointments
- Peripheral neuropathy is the commonest disorder of the PNS
- 2-7% of the general population
- >10% of the elderly

# Definition – the Toronto consensus

- Two of the following
- Neuropathic symptoms
- Decreased distal sensation
- Decreased/absent ankle jerks



- Study in Nueces County, Texas (the town of Corpus Christi, population about 350,000)
- 4890 charts evaluated
- 458 included in study

# Diagnoses

- About 80% were given a specific diagnosis
- 2/3 before seeing a neurologist and 15% after diagnostic testing
- Diabetes, thyroid disease, alcohol, chemotherapy, B12 deficiency, paraproteinemia

# It's all about the sugars

- 9.1% of the US population is diabetic (Waldfoegel et al 2017 )
- 29.1 million individuals
- 30-50% will develop symptoms of diabetic peripheral neuropathy (DPN)

# Treatment

- \*there is no treatment for numbness\*
- Treatment is based first on treating any underlying medical condition
- Pain management is the keystone of therapy

# Treatment

- What is the best treatment for neuropathic pain?
- What proof do I have that my treatments work?

# But there's always a problem

- Most studies involve small numbers of patients
- Duration is typically 4-12 weeks
- 25% of patients respond to placebo/no therapy
- Definition of success is a 30-50% reduction in pain

# Antidepressants

- Amitriptyline (Elavil)
- Nortriptyline (Aventyl)
- Duloxetine (Cymbalta)
- Venlafaxine (Effexor)

# Anticonvulsants

- Pregabalin
- Gabapentin
- Valproic acid



# Local creams

- Capsaicin
- Others

# Opioids

- 2009 systematic review of opioids for chronic noncancer pain found little evidence of longterm effectiveness and a high risk of abuse, addiction and overdose

# Combination Therapy – Nortriptyline and Gabapentin

- A randomised trial of 47 patients – most with diabetic neuropathy
- Four weeks of therapy
- Average dose nortriptyline 50mg and gabapentin 2180mg

# Marijuana

- Long history in Eastern medicine
- First used by Dr William O'Shaughnessy in 1841
- Widely used in North America in the late 19<sup>th</sup> century
- Largely banned in the west by the 30's and 40's

# So is there any evidence?

- **Cannabis-based medicines for chronic neuropathic pain in adults.**
- [Mücke M](#)<sup>1</sup>, [Phillips T](#), [Radbruch L](#), [Petzke F](#), [Häuser W](#).
- **A Cochrane Review**

- Review was performed in November 2017
- Published March 7th 2018
- All randomised trials
- 16 studies, 1750 patients
- 2-26 weeks
- Nasal spray, pill, inhalation
- 15 vs placebo, 1 vs dihydrocodeine

# Study Quality

- Low in two studies
- Moderate in 12
- High in 2
- Based on the risk of bias
- Overall quality low to moderate

# Primary Outcome

- Cannabis may increase the number of patients achieving 50% pain control vs placebo
- Higher risk of adverse events resulting in study withdrawal on Cannabis (10% vs 5%)



# Toward Optimized Practice

## TOPALBERTADOCTORS

- Ranked all therapies for neuropathic pain
- Amitriptyline was most effective
- Cannabinoids were the least effective
- Documented side-effects in many patients

# Genetic Neuropathies

- Commonest is Hereditary Motor and Sensory Neuropathy ( but always called Charcot-Marie-Tooth Disease)
- Gene frequency about 1:2000
- Family of genetic diseases – at least 80+ different genes
- A demyelinating neuropathy

# Genetic Neuropathies

- Gene frequency of well-described neuropathies about 1:1000
- Genetics probably plays a role in many other patients
- Can present late

