



# Neuropathic Pain in Recessive Dystrophic Epidermolysis Bullosa (RDEB)

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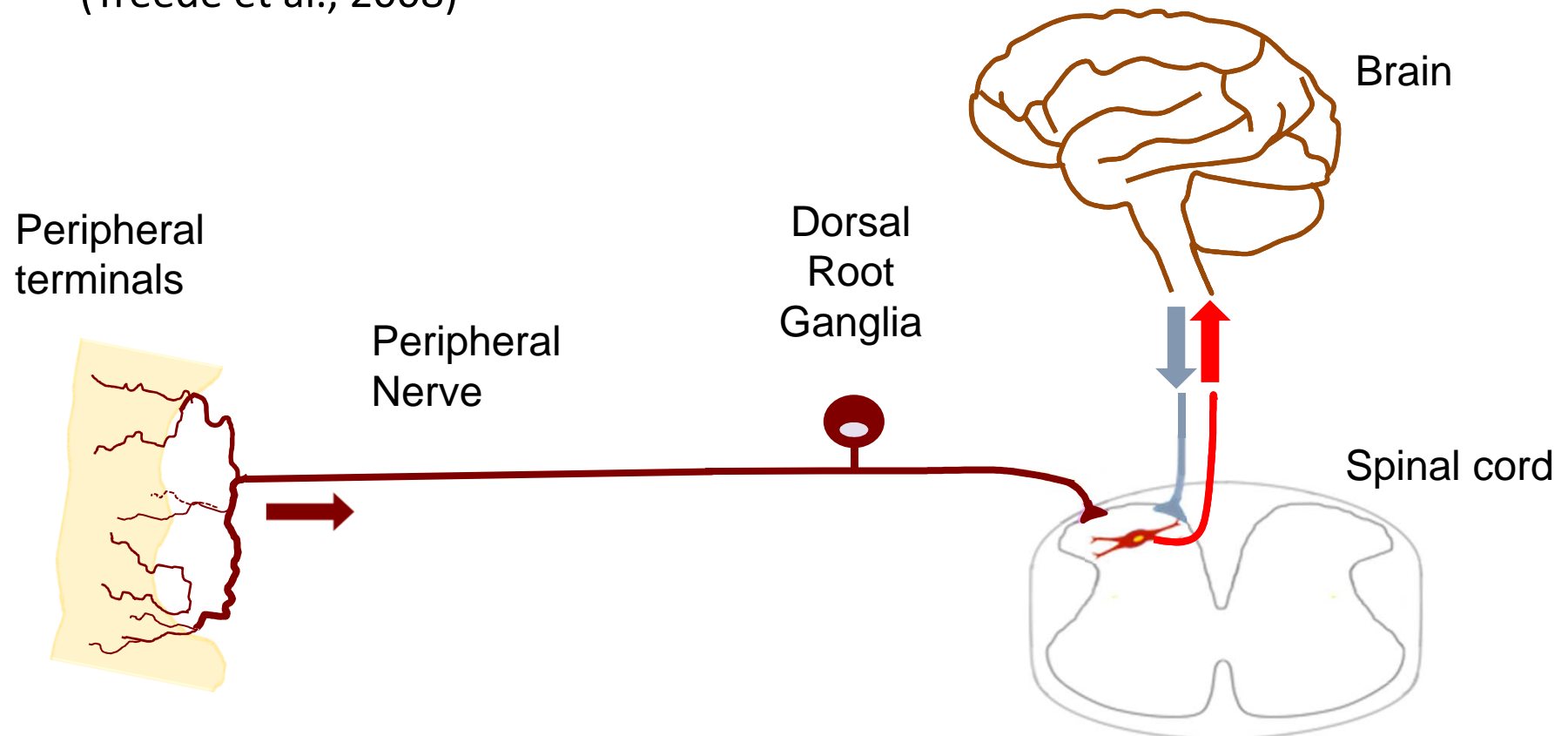


# Pain in RDEB

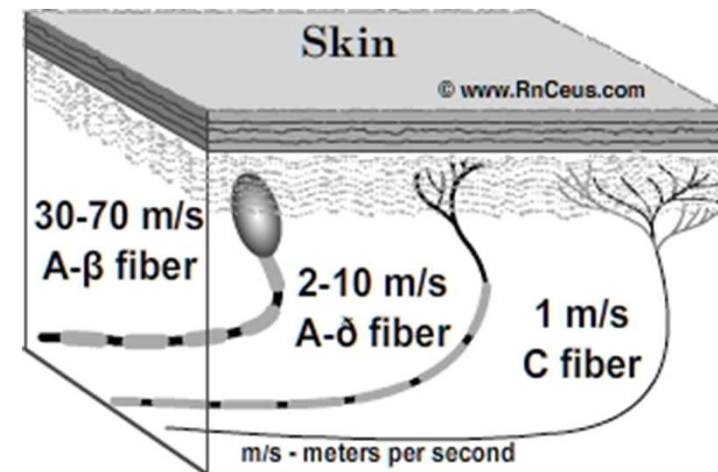
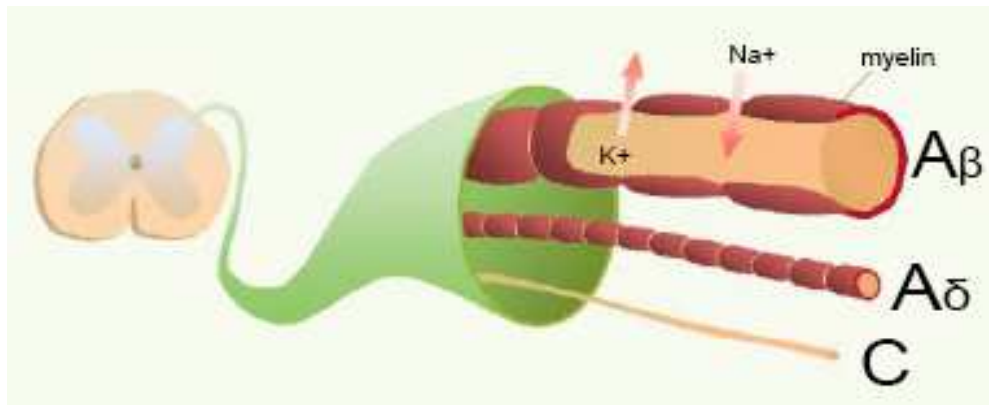
- At least 50% of RDEB patients suffer from intense pain (Fine et al., 2004).
- Chronic pain can be inflammatory, musculoskeletal, or neuropathic
- Treatment for neuropathic pain is different from other chronic pains.

# Neuropathic pain

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



# Somatosensory fibres in the skin



**TABLE 10-5** Classes of Somatosensory Nerve Fibers

FIBER TYPE	FIBER CHARACTERISTICS	SPEED OF CONDUCTION	ASSOCIATED WITH
A $\beta$ (beta)	Large, myelinated	30–70 m/sec	Mechanical stimuli
A $\delta$ (delta)	Small, myelinated	12–30 m/sec	Cold, fast pain, mechanical stimuli
C	Small, unmyelinated	0.5–2 m/sec	Slow pain, heat, cold, mechanical stimuli

# Aim of the study

- To investigate if RDEB patients have neuropathic pain
- and if yes, to find what was causing it (neuropathy)

# Results

- We enrolled 29 adult RDEB patients (COL7A1) and 27 age/gender matched controls
- 92.8% have pain every day
- Acute pain occurs localised to areas of active skin blistering and resolves following healing



# Pain in RDEB

- However, in addition patients also describe persistent pain coming from areas of skin not actively injured, and especially localised to the feet



# Characterization of persistent pain in uninjured skin

- A high prevalence of descriptors suggestive of neuropathic pain
- DN4 questionnaire (screening tool) (Bouhassira et al., 2005).
- Numbness, itching, pins and needles, burning, tingling and electric shocks sensations

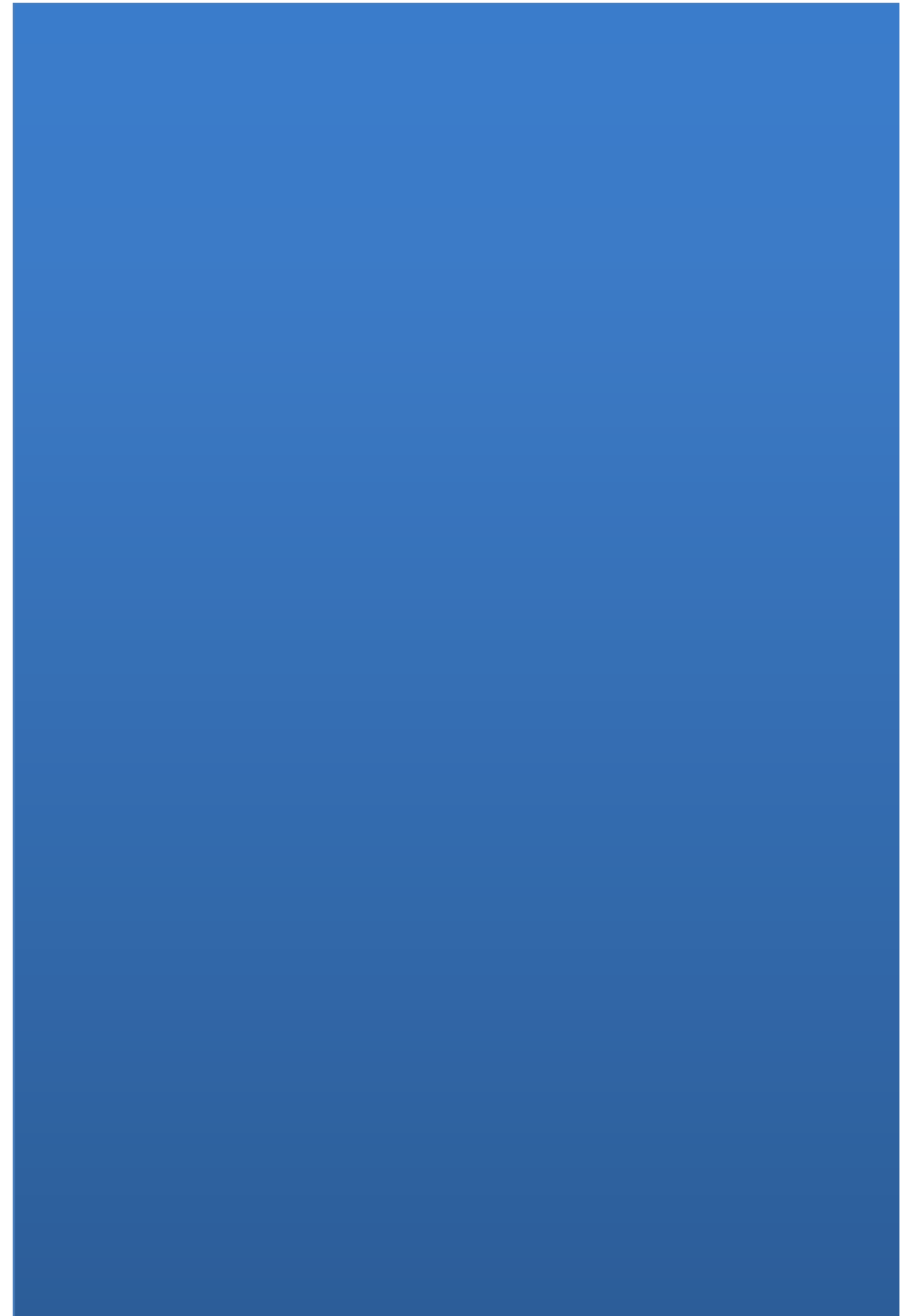
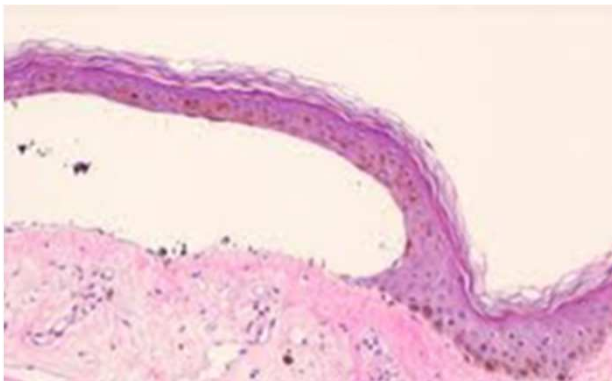
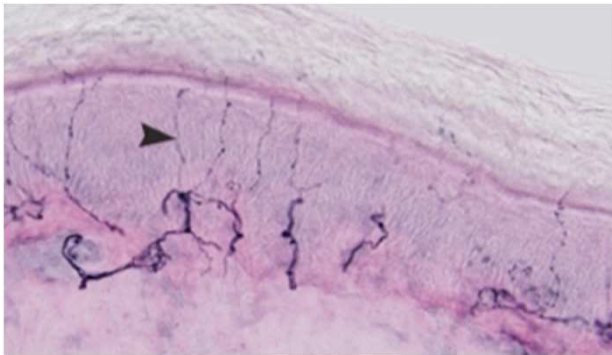




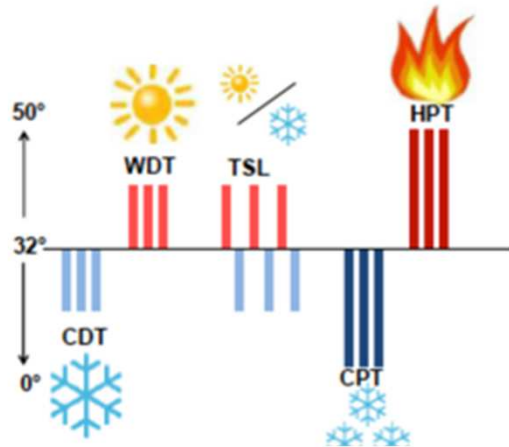
If there is neuropathic pain, where  
is the neuropathy?

- **Small (A $\delta$ /C fibres) dysfunction**

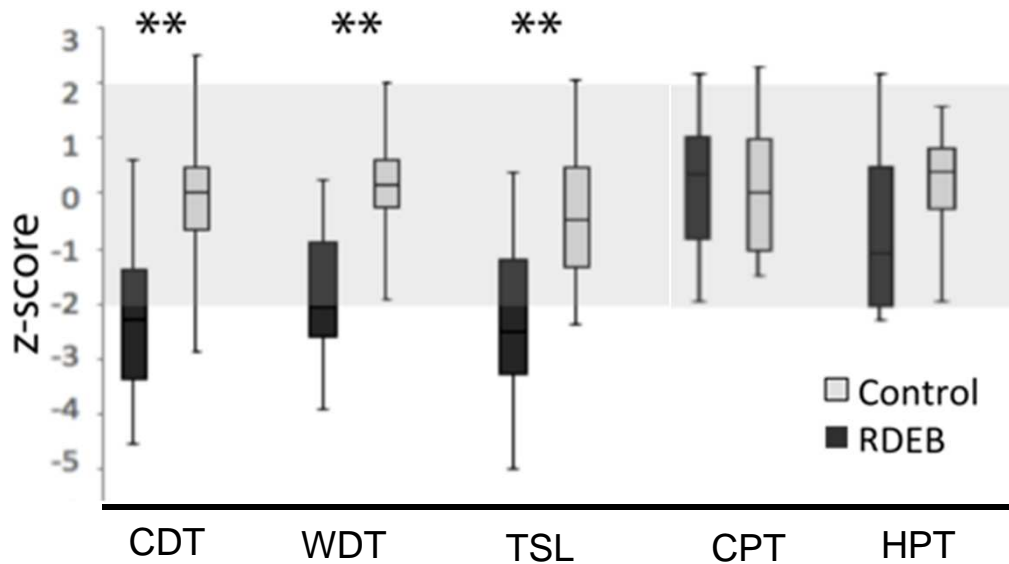
Hypothesis: fibres in the epidermis will be damaged with repetitive episodes of blistering and healing



# Small fibre function (A $\delta$ /C): Quantitative Sensory Test



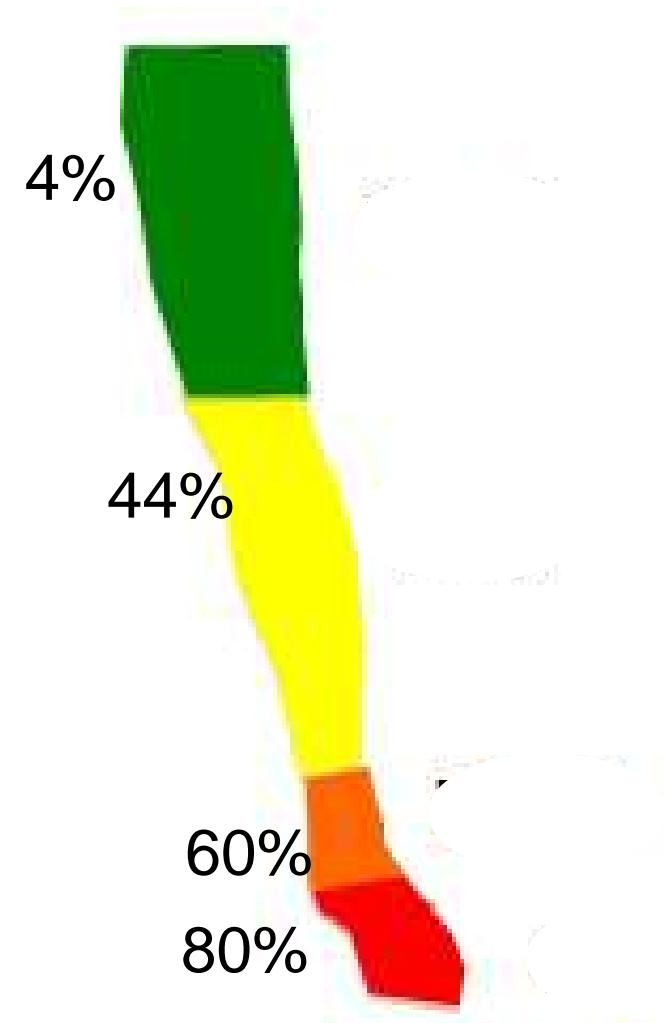
1/3 of patients had paradoxical heat sensations



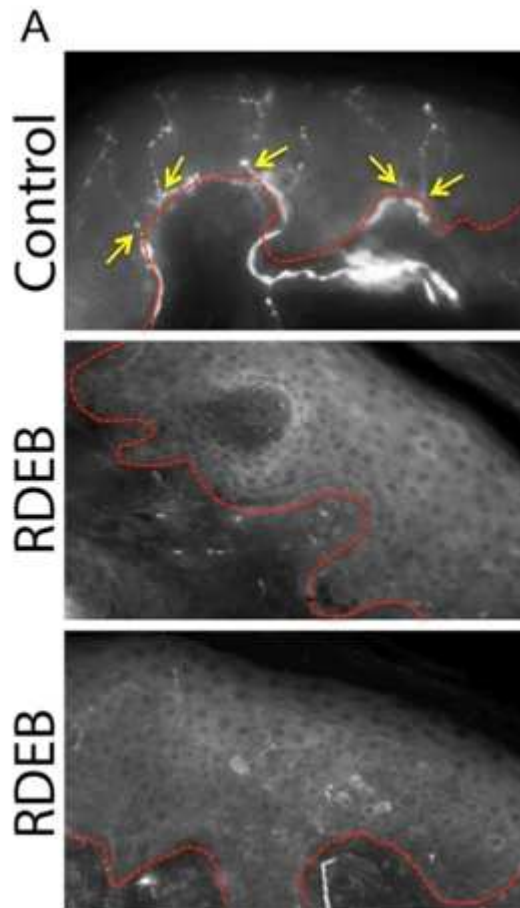
German Research Network on Neuropathic Pain (DFNS)

# Small fibre neuropathy

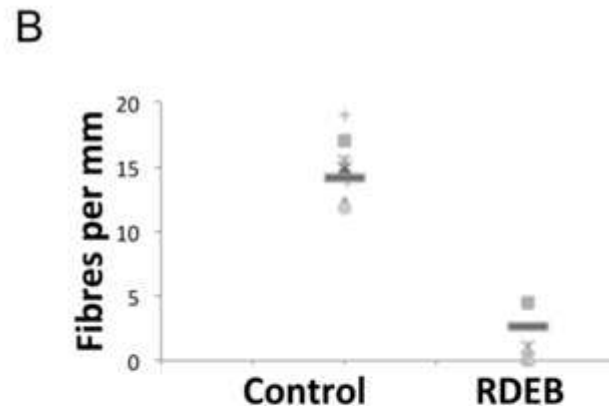
- Clinical examination showed nerve dysfunction was present in a length dependent distribution
- Only 16% have it in the hands



# Intraepidermal nerve fibre density (C fibres)



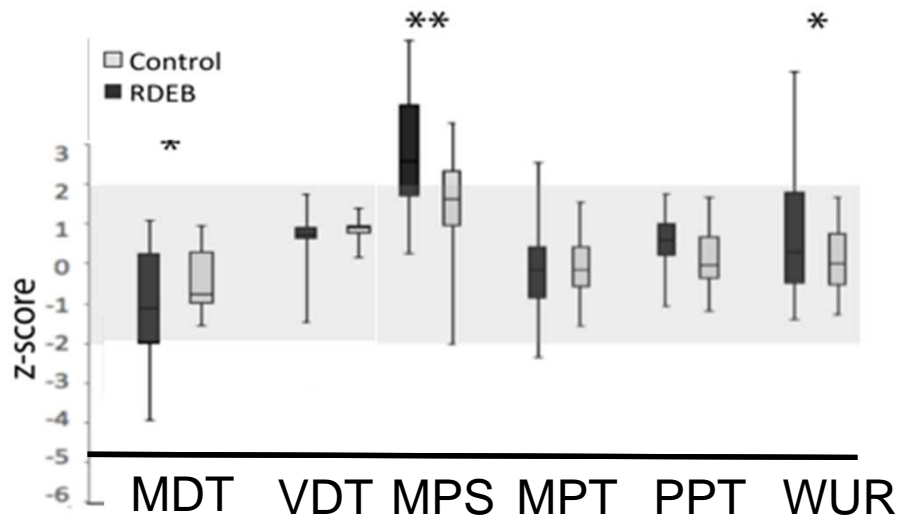
IF PGP9.5



- 3mm biopsy from unwounded skin
- 10 cm above the external malleolus (reference values Provitera et al 2016)

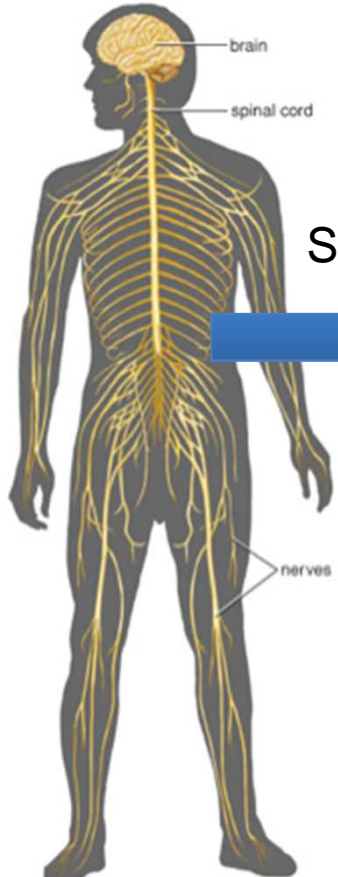
# Large fibre function (A $\beta$ ): nerve conduction and Quantitative Sensory Test

	Sural nerve	
	SNAP ( $\mu$ V)	NCV (m/s)
Controls	23.3 $\pm$ 1.6	50.9 $\pm$ 1.7
RDEB	18.4 $\pm$ 2.3	51.7 $\pm$ 1.7
p value	0.08	0.7

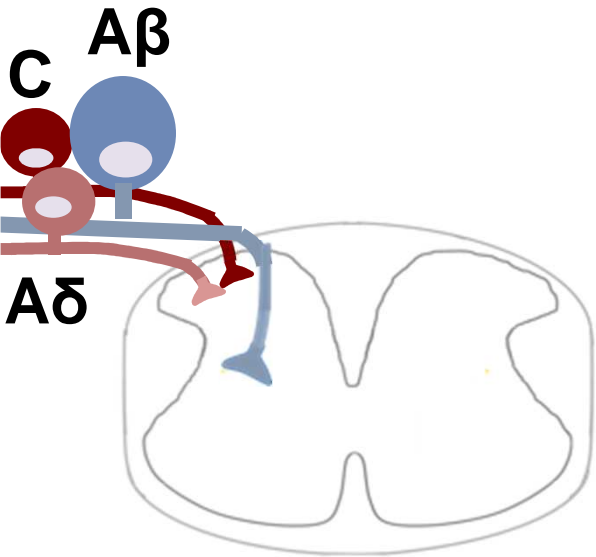
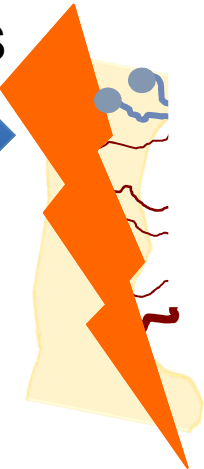


Large A $\beta$  fibres were not affected

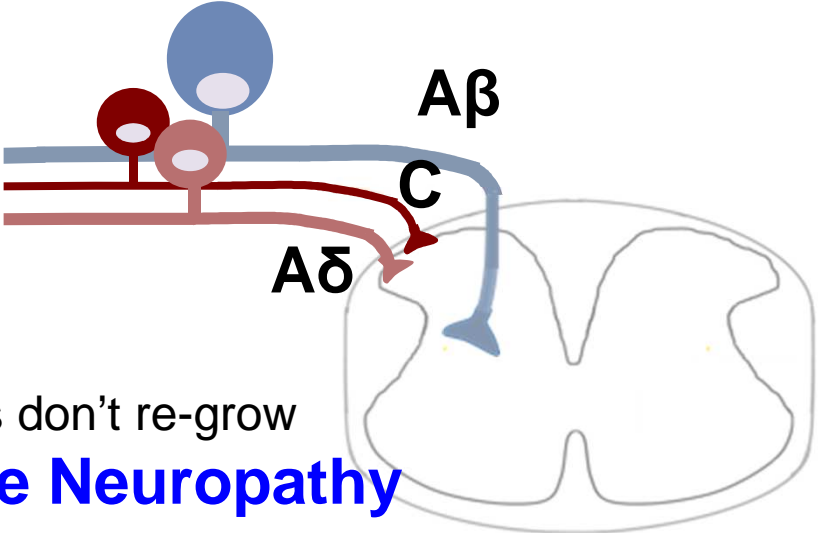
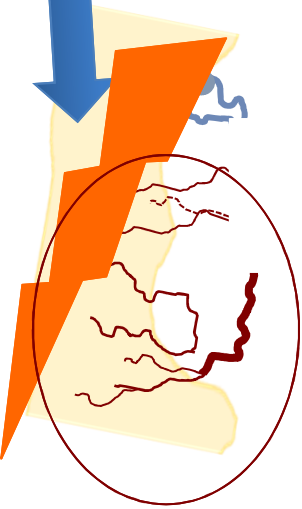
# CONCLUSION



SHORT AXONS



LONG AXONS



Small fibres of long axons don't re-grow  
**Painful Small Fibre Neuropathy**

# TAKE HOME MESSAGE:

- RDEB patients are at high risk of developing neuropathic pain
- Test your patients using the DN4 questionnaire (S :82% S:73% )
- Treat them accordingly



# Acknowledgements



## Recessive dystrophic epidermolysis bullosa results in painful small fibre neuropathy

Sofia von Bischoffshausen,<sup>1</sup> Dinka Ivulic,<sup>2</sup> Paola Alvarez,<sup>2</sup> Victor C. Schuffeneger,<sup>2</sup> Juan Idiaquez,<sup>4</sup> Constanza Fuentes,<sup>3,4</sup> Pilar Morande,<sup>2</sup> Ignacia Fuentes,<sup>5,4</sup> Francis Palisson,<sup>5,6,7</sup> David L. H. Bennett<sup>8</sup> and Margarita Calvo<sup>3,9</sup>

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International Association for the Study of Pain

**IASP**

Working together for pain relief