Hunting for signs of demyelination

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Demyelination can be distinguished by EDX, but requires:

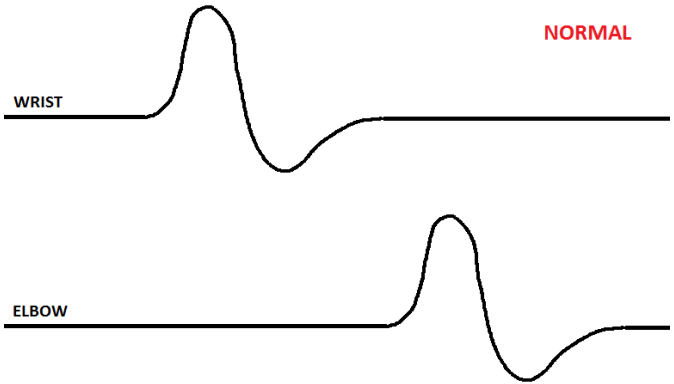
- Careful nerve stimulation
- Wise selection of techniques and nerves
- Temperature control
- Knowledge of pitfalls
- Knowledge of different features between blocking and temporal dispersion

Careful nerve stimulation

- In some cases, EMG reports exhibit stimulations with 99.9mA throughout all examinations → quick, dirty, painful and prone to artefacts!
- However, in demyelinating diseases higher stimulation intensities for supramaximal stimulation might be needed.
- The following hints apply to motor and sensory nerve conduction studies (NCS)

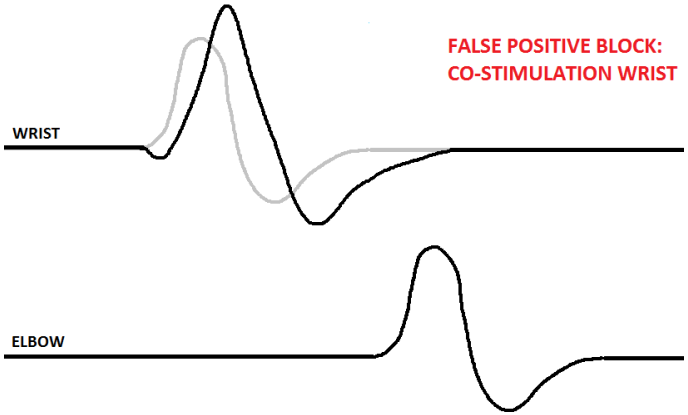
Nerve stimulation, correct stimulus intensity

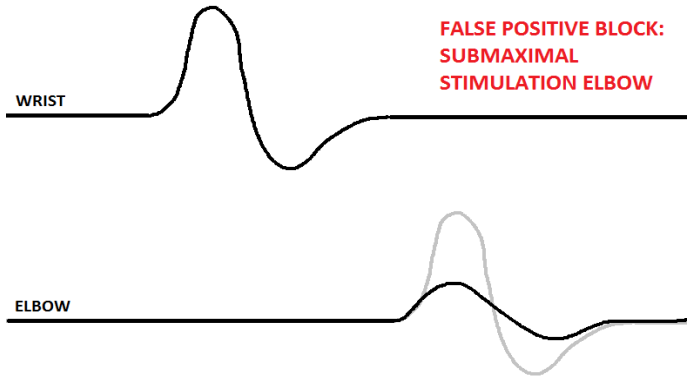
(Disclosure: figures stolen and implemented from Hessel Franssen 2016)



Nerve stimulation, correct stimulus intensity

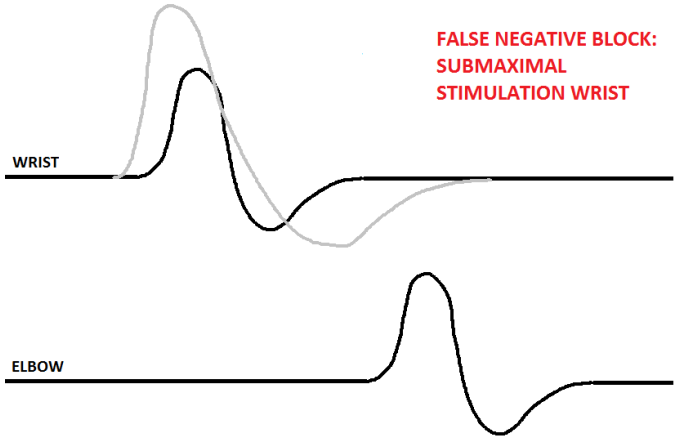
False positive blocking





Nerve stimulation, correct stimulus intensity

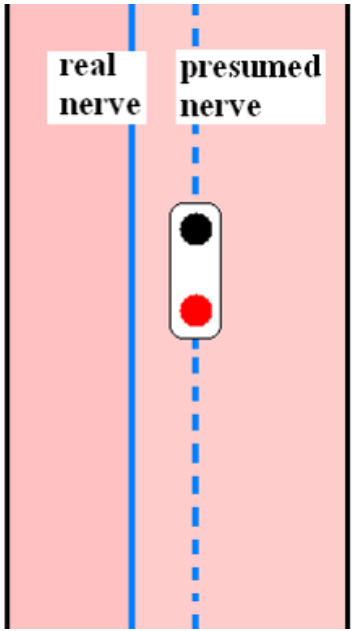
False negative blocking

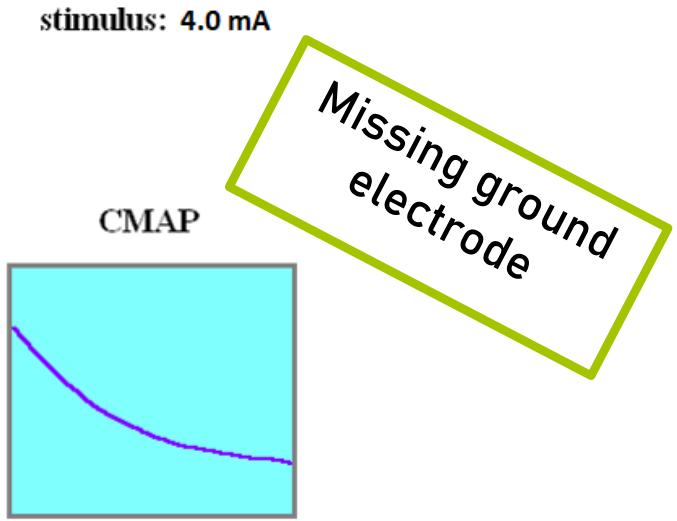


Nerve stimulation, adjusting stimulator

First stimulus with 4.0mA

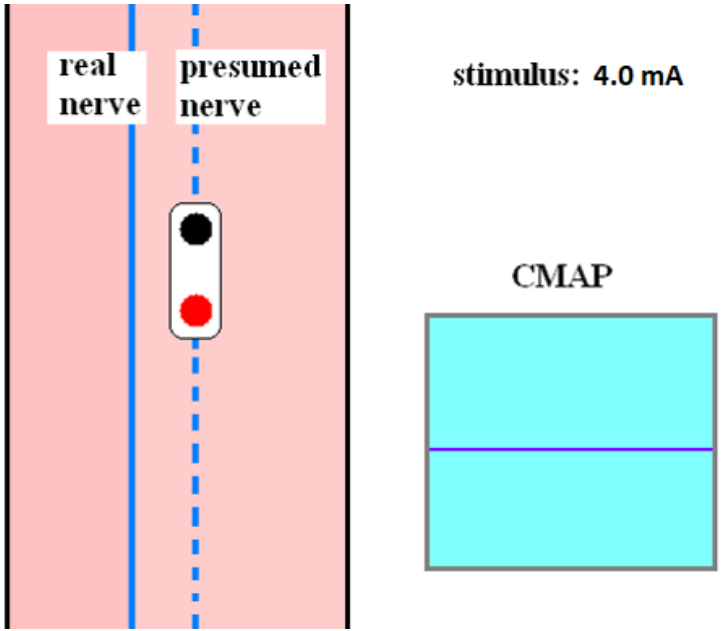
What is wrong here?? (hint: look at CMAP)





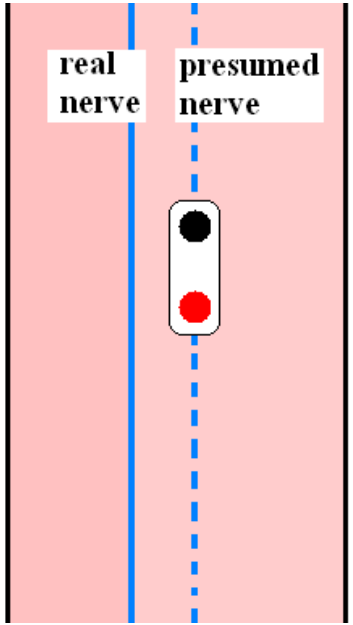
Nerve stimulation, adjusting stimulator

Second stimulus with 4.0mA
Now better! Ground electrode placed



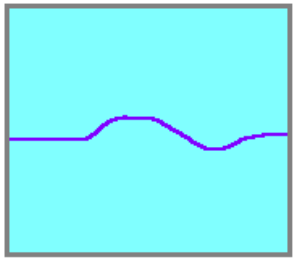
Nerve stimulation, adjusting stimulator

Third stimulus with 5.0mA
First muscle response… and now?



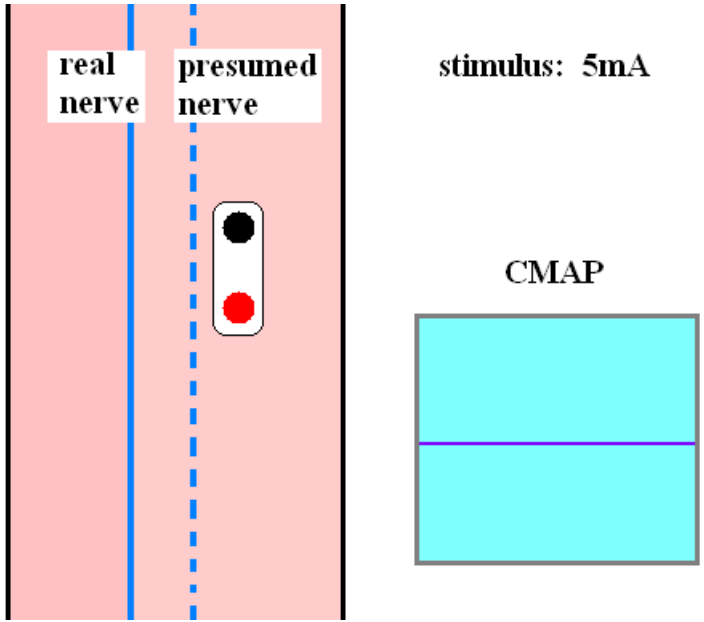
stimulus: 5mA

CMAP



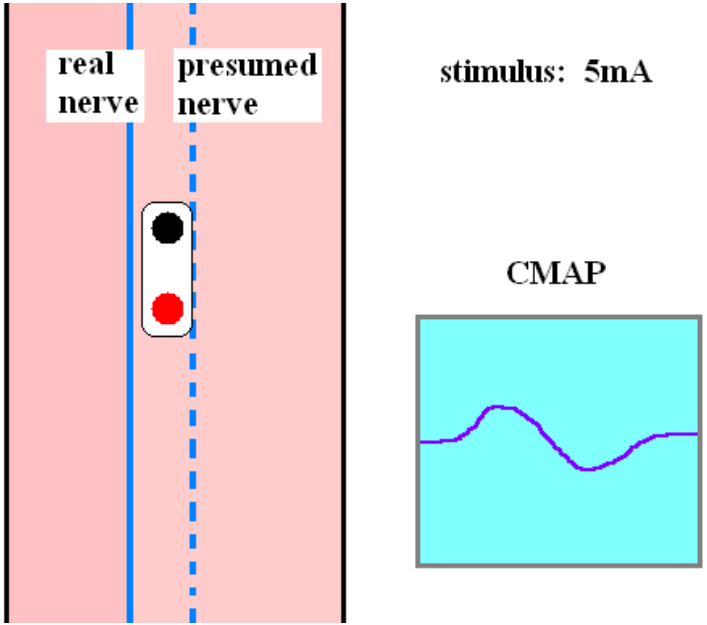
Nerve stimulation, adjusting stimulator

Fourth stimulus with 5.0mA
Move stimulator… bad choice



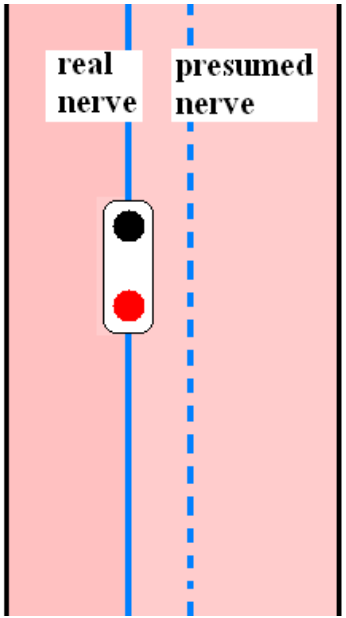
Nerve stimulation, adjusting stimulator

Fifth stimulus with 5.0mA
Move stimulator… much better CMAP



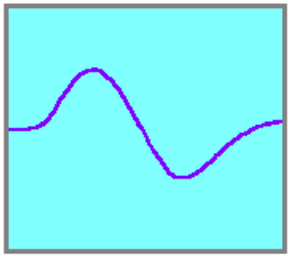
Nerve stimulation, adjusting stimulator

Sixth stimulus with 5.0mA
Move stimulator… great CMAP!



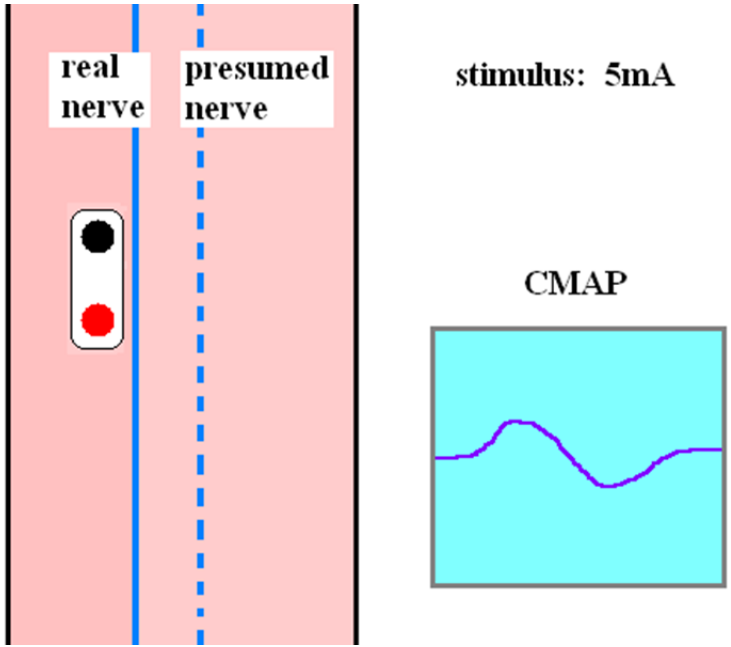
stimulus: 5mA

CMAP



Nerve stimulation, adjusting stimulator

Seventh stimulus with 5.0mA
Move stimulator… worse CMAP! Go back…

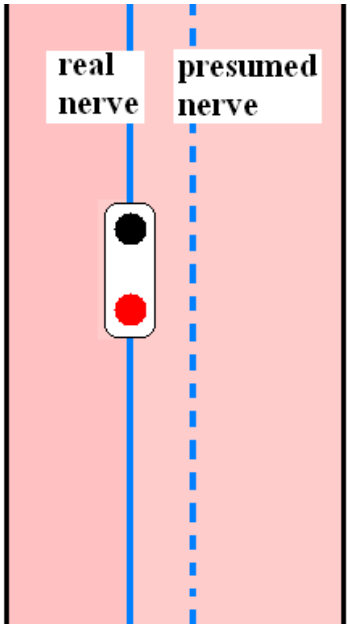


stimulus: 5mA

CMAP

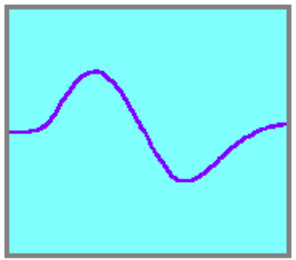
Nerve stimulation, adjusting stimulator

8th stimulus with 5.0mA
Move stimulator… make CMAP great again



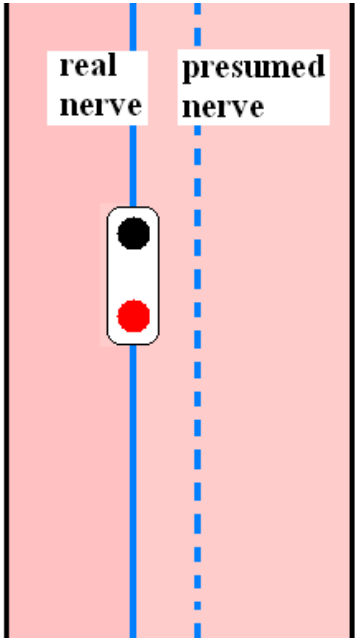
stimulus: 5mA

CMAP



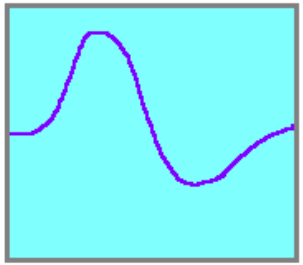
Nerve stimulation, adjusting stimulator

9th to xxth stimulus with increasing mA
Do not move stimulator… increase until MAX + 10% intensity



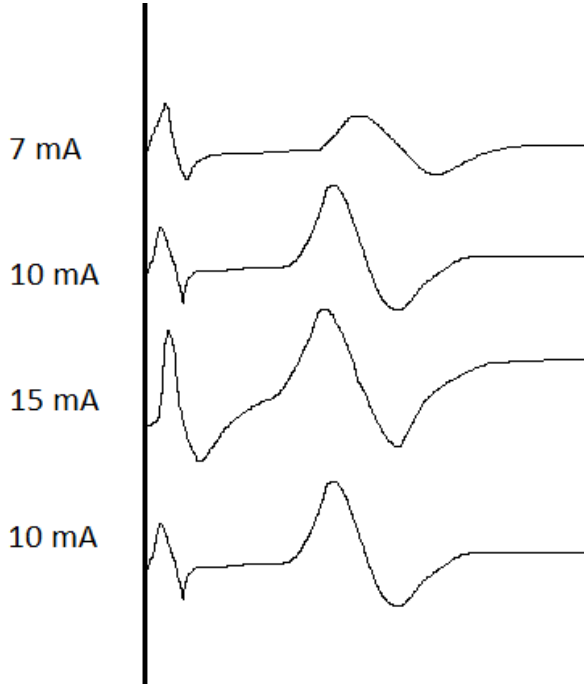
stimulus: 10mA

CMAP



Sensory nerve stimulation, similar approach

- Select optimal position
- Increase stimulation until maximum amplitude
- Decrease if stim. artefacts or change stim. mode
- Average with optimal stim…



Temperature control

- Temperature has a dual impact, locally on CMAP/SNAP amplitude and segmental on conduction velocity.

- Decrease in temperatur ***increase*** CMAP/SNAP amplitude to 1-2% per °C
  → in real life, clinically rarely meaningful
  → however, cold temperatur can e.g. reduce decrement in Myasthenia
  → cold temperature can reduce relative blocking

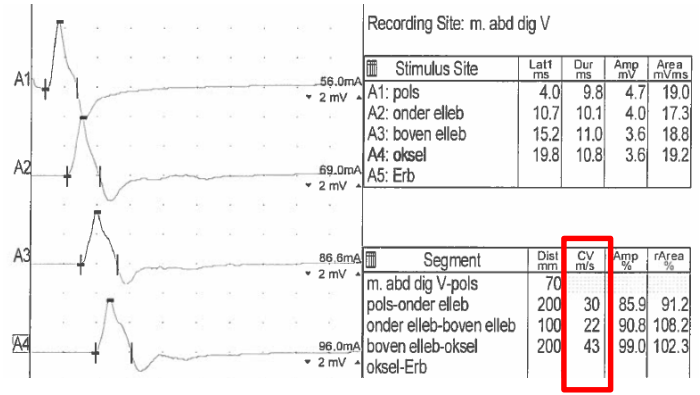
  - Segmental NCS velocity increases 1.2 to 2.4m/s per °C (Dioszeghy and Stålberg, 1992)
    - Correction factors like 2.2m/s/°C only valid for «normal» arm nerves (de Jesus 1973)

  - Superficial sensory nerves are more susceptible to temperature compared to deeper motor nerves

Temperature: cold → slowing

(Franssen 2016)

- Before warming
- DML slowing
- Severe MCV slowing forearm
- Severe MCV slowing elbow
- MCV slowing upper arm
- → generalized slowing

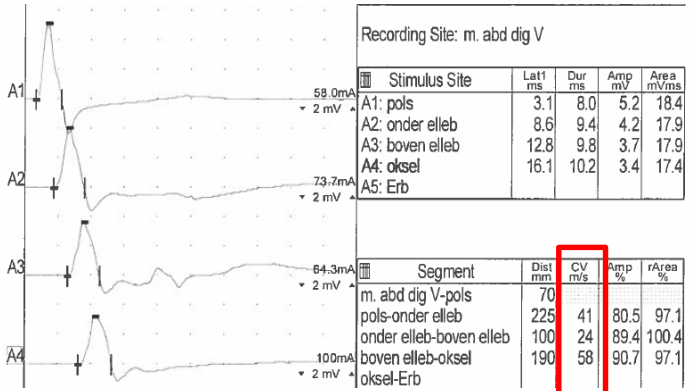


Recording Site: m. abd dig V

Stimulus Site	Lat1 ms	Dur ms	Amp mV	Area mVms
A1: pols	4.0	9.8	4.7	19.0
A2: onder elleb	10.7	10.1	4.0	17.3
A3: boven elleb	15.2	11.0	3.6	18.8
A4: oksel	19.8	10.8	3.6	19.2
A5: Erb				

Segment	Dist mm	CV m/s	Amp %	rArea %
m. abd dig V-pols	70			
pols-onder elleb	200	30	85.9	91.2
onder elleb-boven elleb	100	22	90.8	108.2
boven elleb-oksel	200	43	99.0	102.3
oksel-Erb				

- After warming to 37°C
- MCV slowing forearm
- Severe MCV slowing at elbow
- → focal slowing



Recording Site: m. abd dig V

Stimulus Site	Lat1 ms	Dur ms	Amp mV	Area mVms
A1: pols	3.1	8.0	5.2	18.4
A2: onder elleb	8.6	9.4	4.2	17.9
A3: boven elleb	12.8	9.8	3.7	17.9
A4: oksel	16.1	10.2	3.4	17.4
A5: Erb				

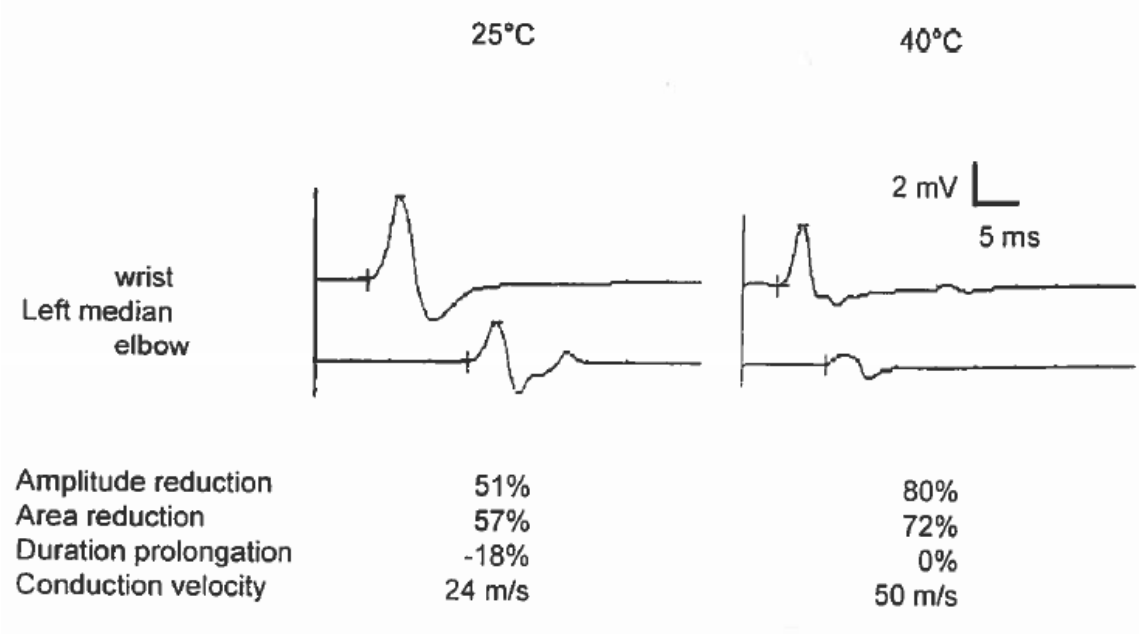
Segment	Dist mm	CV m/s	Amp %	rArea %
m. abd dig V-pols	70			
pols-onder elleb	225	41	80.5	97.1
onder elleb-boven elleb	100	24	89.4	100.4
boven elleb-oksel	190	58	90.7	97.1
oksel-Erb				

Temperature: effect on blocking, example

(Franssen 2016)

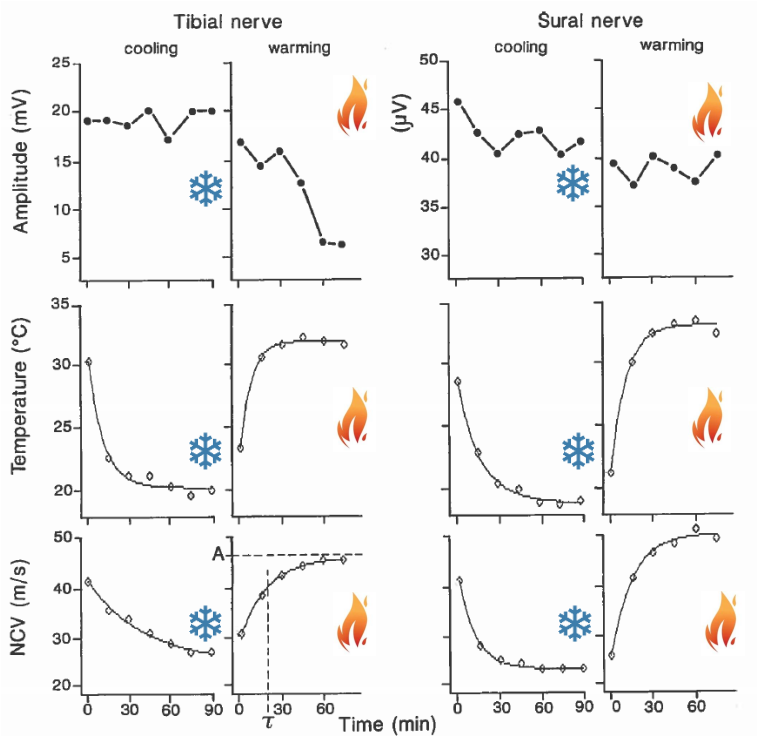
- Segmental CMAP drop (area)
- 25°C → 57%
- 40°C → 72%

(Franssen 1999)



Temperature: effect on amplitude and velocity

(Franssen 1999)

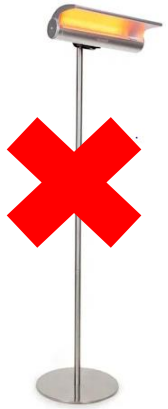


Temperature: how to control temperature

- Ask patients to wear gloves and warm underwear/boots to avoid cool extremities
- Ask patients to come somewhat earlier to warm-up in the waiting room
- Heat the waiting room and examination room appropriately
- Use warm blankets for longer examinations to avoid cooling of limbs
- In very cold hands/feet → warm water bath

Temperature: how NOT to control temperature

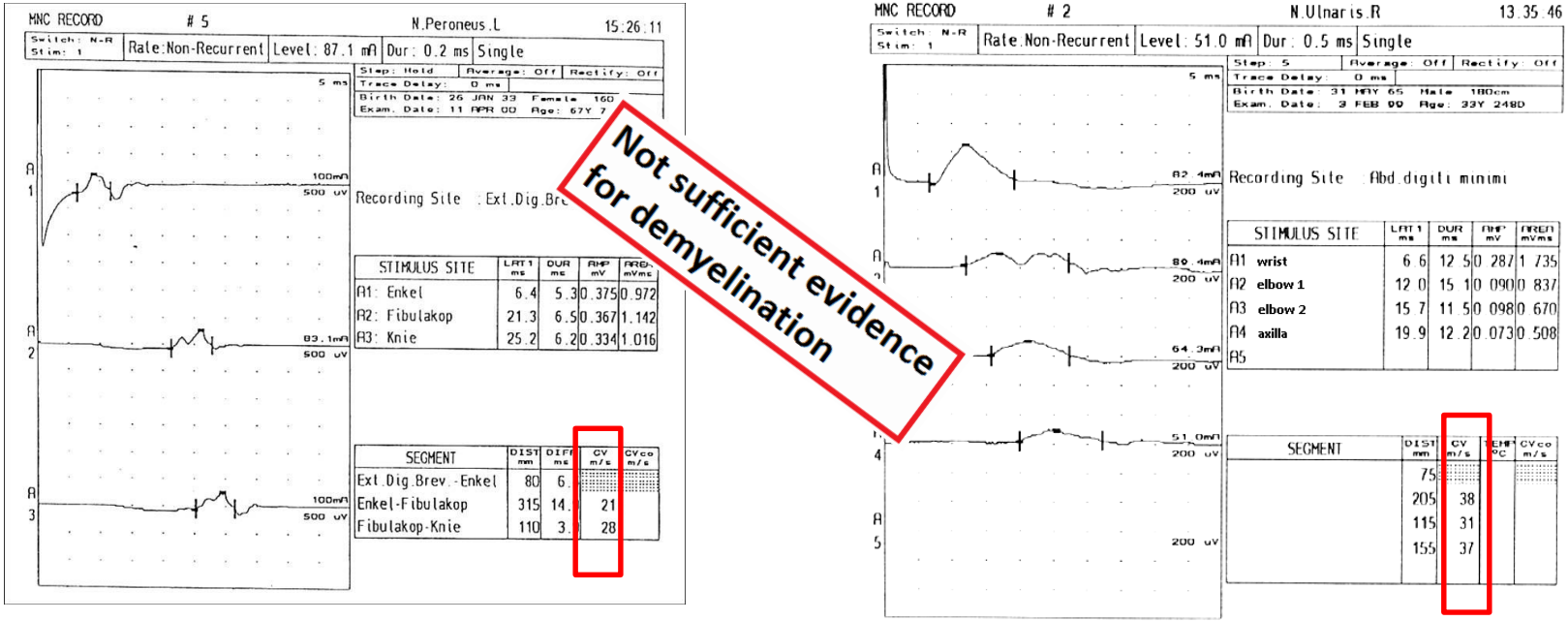
- Infrared heater?
  - → roasts skin only, not deeper tissue
  - → roasts patient
  - → roasts examiner
  - → heats room
  - → sweating bad for self-adhesive electrodes



- Can be used for more appropriate applications…

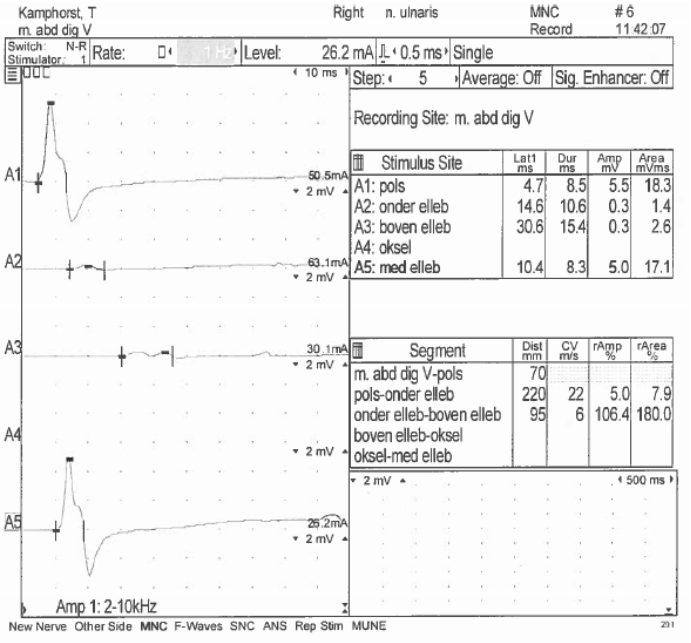
Pitfalls while hunting… (1) Low CMAP

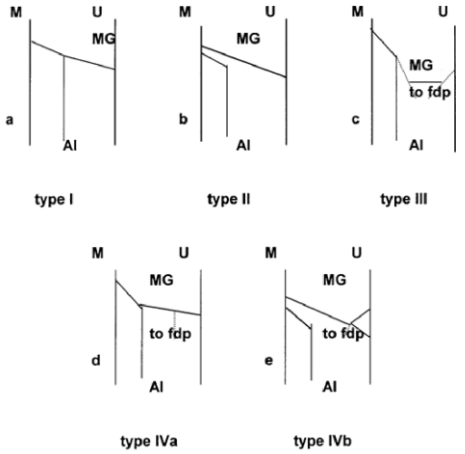
- Very low CMAP amplitude, e.g. <1mV
  → axonal loss of fast conductiong fibres leads to segmental slowing



Pitfalls while hunting… (2) Martin Gruber

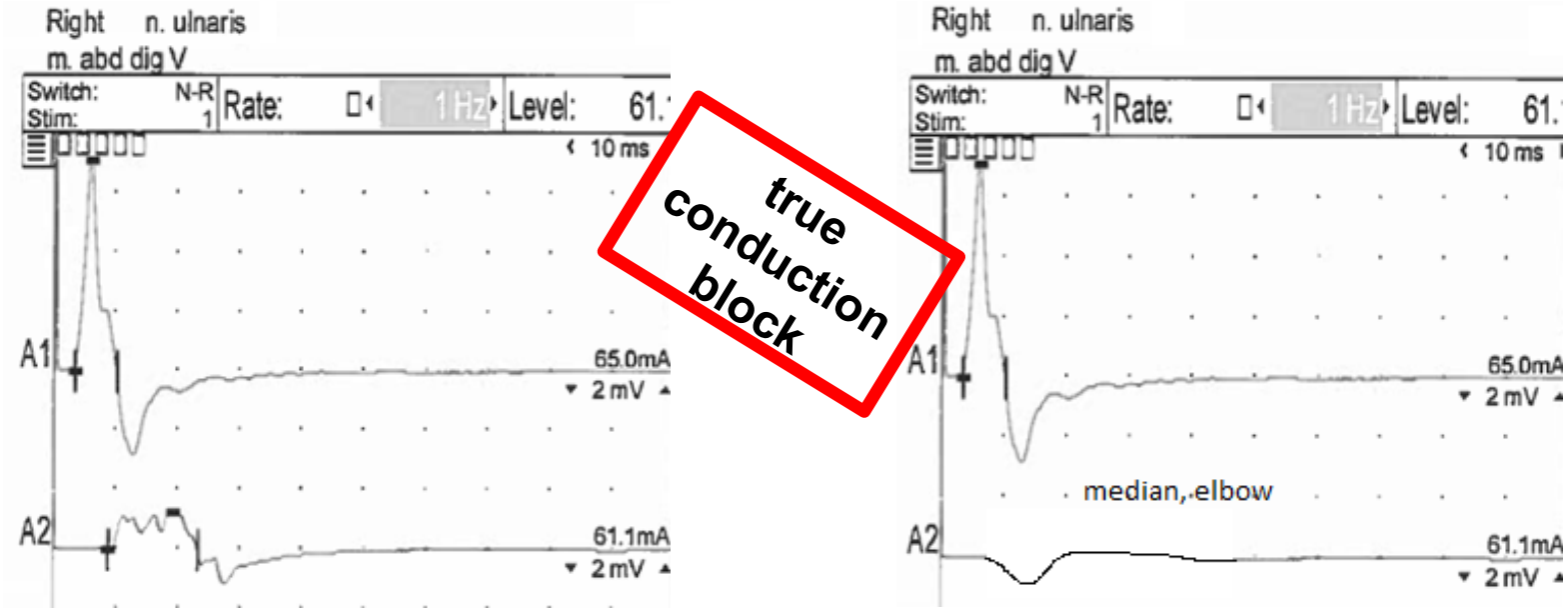
- Estimated prevalence 15-20% in EDX and 22% cadaver studies
- In every fifth MG-A bilaterally Rodrigez-Niedenführ et al. 2002
- 4 major types defined



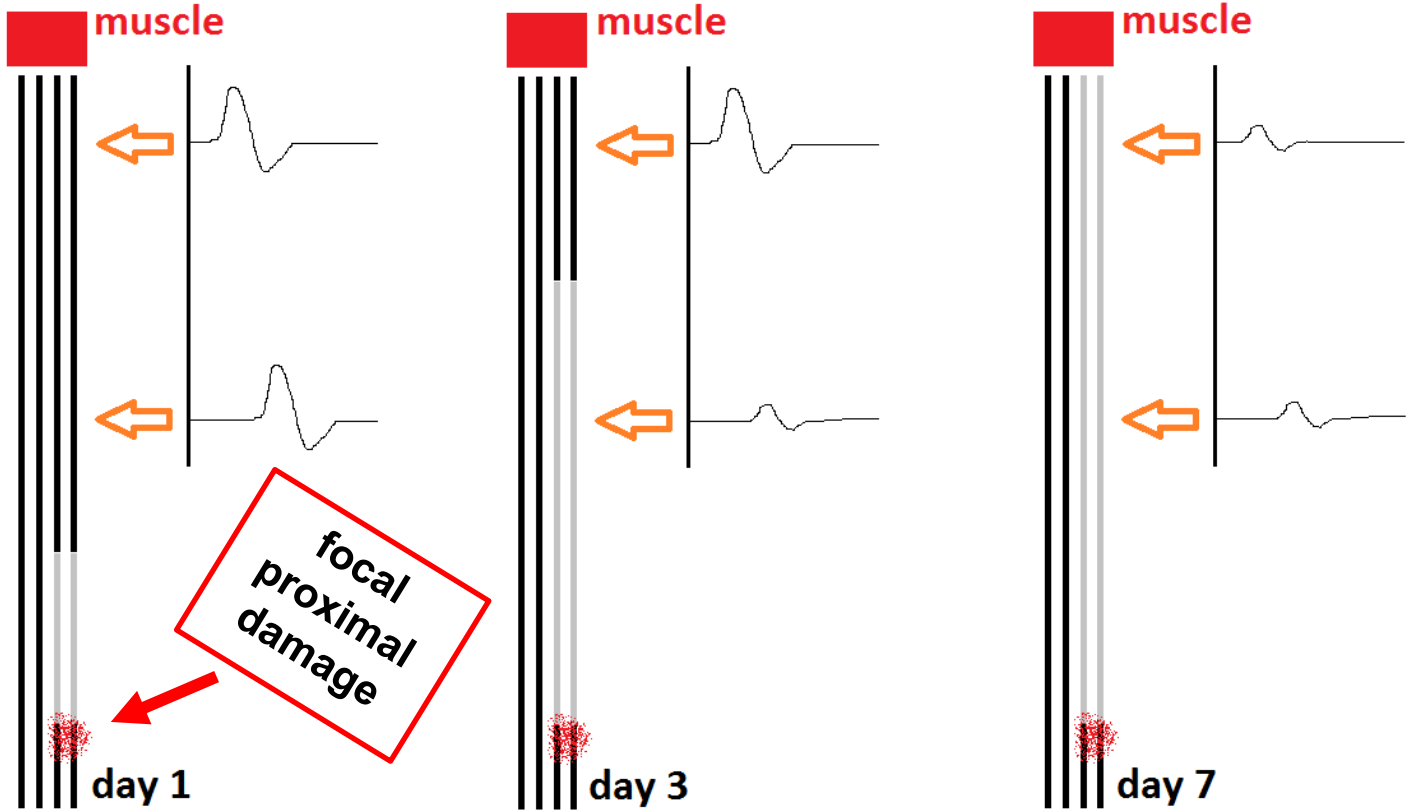


Pitfalls while hunting… (2) Martin Gruber or block?

- True conduction block of ulnar nerve?
- → stimuation of median nerve at ellbow evokes no CMAP or with positive deflection



Pitfalls while hunting… (3) Wallerian degeneration



Summary pitfalls

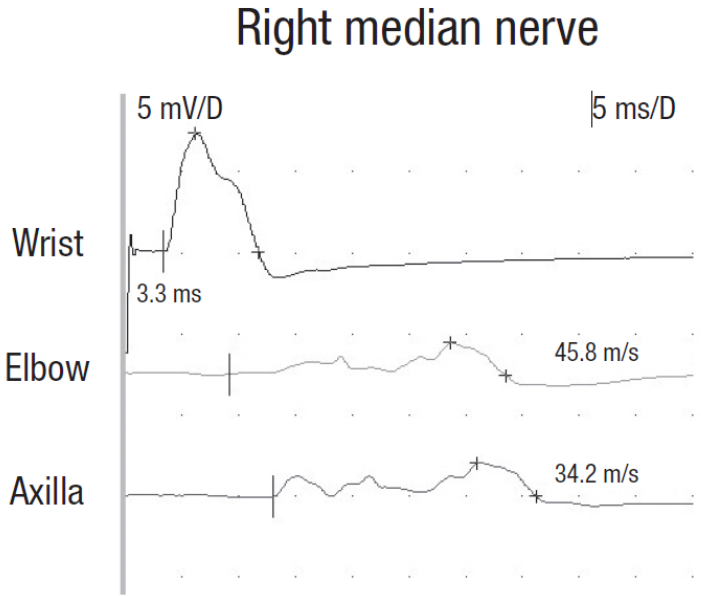
- If CMAP is very low → be careful when judging demyelination
  →slowing of NC velocity secondary to severe axonal loss is no genuine demyelination

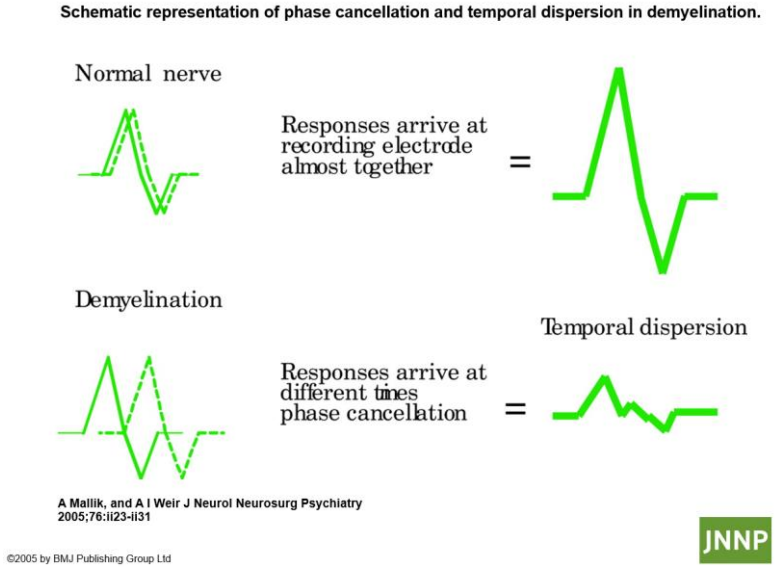
- Ulnar CMAP drop in forearm → think of Martin Gruber Anastomosis and check

- Remember Wallerian degeneration in acute diseases, repeat NCS if necessary
  → e.g. sudden weakness with normal CMAP amplitude in an weak muscle
  → early Wallerian degeneration or proximal conduction block (e.g. MMN)

Conduction block vs. temporal dispersion

- Example of severe temporal dispersion in Lewis-Sumner syndrome

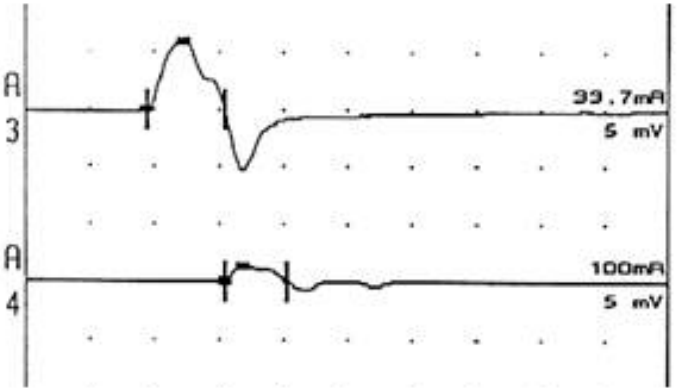


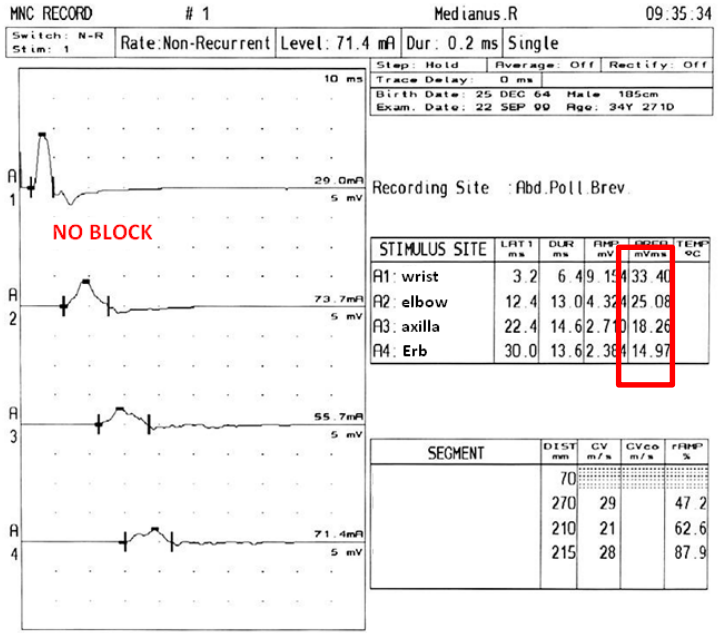


Conduction block vs. temporal dispersion

- Drop of max. CMAP amplitude does not neccessarily mean CB
- → drop of area instead of amplitude can be helpful to distinguish

- However, phase cancellation in TB reduces area





Conduction block vs. temporal dispersion

- Can clinical features help for diagnostic or prognostic aspects?

(in addition to a choice of several existing criteria?)

→Blocking leads to clinical weakness

→Slowling/temporal dispersion rarely weakness

→Block: IVIG response likely (81%)

→E.g. Intratect®, Kiovig®, Octagam®, Privigen® etc

→Only slowing/TP IVIG response more unlikely (11%)

Multifocal Motor Neuropathy: Diagnostic Criteria that Predict the Response to Immunoglobulin Treatment

R. M. Van den Berg-Vos,* H. Franssen,† J. H. J. Wokke,* H. W. Van Es,‡ and L. H. Van den Berg*

As multifocal motor neuropathy (MMN) is a potentially treatable disorder, its differentiation from lower motor neuron disease is important. Evidence of conduction block (CB) is considered one of the relevant criteria for the diagnosis of MMN. Strict criteria for CB may lead to underdiagnosis of MMN, however. Using a standardized examination, we studied the clinical, laboratory, and electrophysiological characteristics of 37 patients presenting with a lower motor neuron disorder and electrophysiological features compatible with segmental demyelination. We propose a set of clinical, laboratory, and electrophysiological criteria for the diagnosis of MMN, which has been verified by follow-up and response to treatment with intravenous immunoglobulins. Based on the clinical, laboratory, and electrodiagnostic features, 21 patients were diagnosed with definite MMN (17 responders), 7 were diagnosed with probable MMN (5 responders), and 9 were diagnosed with possible MMN (1 responder). Age at onset, the number of affected limb regions, and the number of patients with a creatine kinase level greater than 180 U/L were significantly lower in responders than in nonresponders. Elevated anti-GM1 antibodies and definite CB were found significantly more often in responders. The proposed diagnostic criteria may be useful in clinical practice and therapeutic trials.

Van den Berg-Vos RM, Franssen H, Wokke JHJ, Van Es HW, Van den Berg LH. Multifocal motor neuropathy: diagnostic criteria that predict the response to immunoglobulin treatment. Ann Neurol 2000;48:919–926

What about hereditary demyelinating neuropathies?

- Clinical features! Very long history, no acute or sub-acute onset

- Rarely any sensory symptoms, only minor
  → missmatch between severe EDX-findings and mild symptoms
  → patients are able to walk freely, but so sensory answer on EDX

→No temporal dispersion or minor in EDX

→No blocking, homogenous velocity reduction.

→Missmatch between ED findings and clinical presentation in hereditary neuropathies compared to acute/subacute onset neuropathies

Comments? Suggestions? Questions…?