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Electrodiagnosis of Immune Neuropathies

Mark B. Bromberg, MD, PhD

Chief, General Neurology Division
Professor of Neurology
University of Utah
Salt Lake City, Utah

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Role of Electrodiagnostic Studies

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- Best estimate underlying nerve pathology
  - Primary demyelination vs primary axonal vs conduction block (multifocal or focal)
  - May be mixed pattern: Choose primary over secondary pattern
- Nerve conduction – pathology correlation sparse
  - Mostly from sensory nerve biopsies, animal models
- Nerve conduction studies more informative than EMG
  - EMG can document axonal loss, but not amount of loss
  - Cannot distinguish primary vs secondary axonal pathology

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EMG, electromyography.

Why This Talk? – Electrodiagnostic Knowledge

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- 100 neurologists (~half university/~half electrodiagnostic or neuromuscular training)
- Follow guidelines?
  - AAN: 8% not university-affiliated/35% university-affiliated
  - EFNS/PNS 2010: 14% not university-affiliated/12% university-affiliated
  - None: 51% not university-affiliated/27% university-affiliated
- Metrics relied upon?
  - Slow conduction velocity: 88%
  - Prolonged distal latency: 79%
  - Temporal dispersion: 72%
  - Prolonged F-wave latency: 56%
  - Decreased distal response: 51%
  - Decreased recruitment on EMG: 47%
  - Absent distal latency: 36%
  - P-waves/fibrillation potentials: 25%

EAN, European Academy of Neurology; PNS, Peripheral Nerve Society.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268.

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Nerve Conduction Studies Challenging to Sort Out

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- Normal or Abnormal Study?
- Must assess each metric = Interpretation!

Nerve	Amplitude	Distal latency	Duration	Conduction velocity	F-wave latency
Sural (S)	7	3.8		42	
Fibular (M) A Fibular (M) BK	3.2 2.8	4.2	6.2 6.2	 43	53.6
Tibial (M) A	9.1	4.8	6.6		55.1
Median (S) W	27	3.8		42	
Median (M) W Median (M) BE	5.8 5.1	3.9	6.6 6.7	 48	30.1
Ulnar (S) W	18	3.6			
Ulnar (M) W Ulnar (M) BE Ulnar (M) AE Ulnar (M) AX	8.4 8.0 7.9 7.4	3.4	6.2 6.2 6.4 6.6	 47 48 49	29.8

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Why This Talk? – Electrodiagnostic Interpretation

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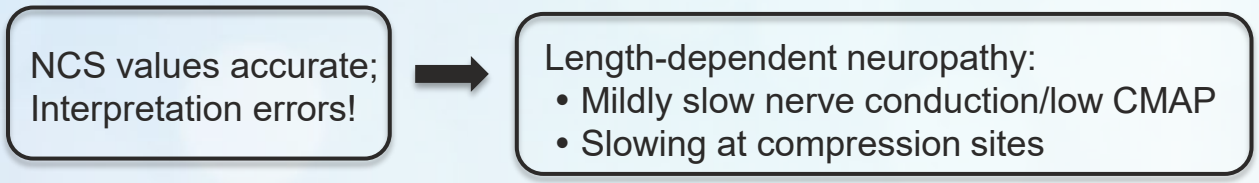
- CIDP overdiagnosis
  - Treat wrong neuropathy
    - 47% did not fulfill criteria for CIDP
      - ALS = 11%
      - Diabetic neuropathy = 11%
      - Idiopathic = 11%
      - Hereditary = 7.5%



- Reasons
  - Failure to consider clinical features
  - Failure to consider slowing due to axonal loss

ALS, amyotrophic lateral sclerosis; CMAP, compound muscle action potential.

Reference: Allen JA. *Neurology.* 2015;85(6):498-504.

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2021 (2nd Revision) EAN/PNS Guidelines

Nerve conduction studies strongly recommended

EAN, European Academy of Neurology; PNS, Peripheral Nerve Society.

Reference: van den Bergh PYK, et al. *J Peripher Nerv Syst*. 2021;26(3):242-268.

Key Points and Outline

- Interpretation: Three key points
  - Assess CMAP amplitude first
  - CMAP waveform (negative slope)
  - Negative peak duration next
  - CMAP waveform shape

- Outline
  - Nerve pathology/physiology
  - Deconstruct CMAP
  - Reconstruct CMAP in setting of pathologies
  - Review ENF/PNS Criteria and simplified guidelines
  - Technical issues
  - Diagnostic challenges

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Nerve Pathology/Physiology

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Axonal, Demyelinating, and Conduction Block Neuropathies

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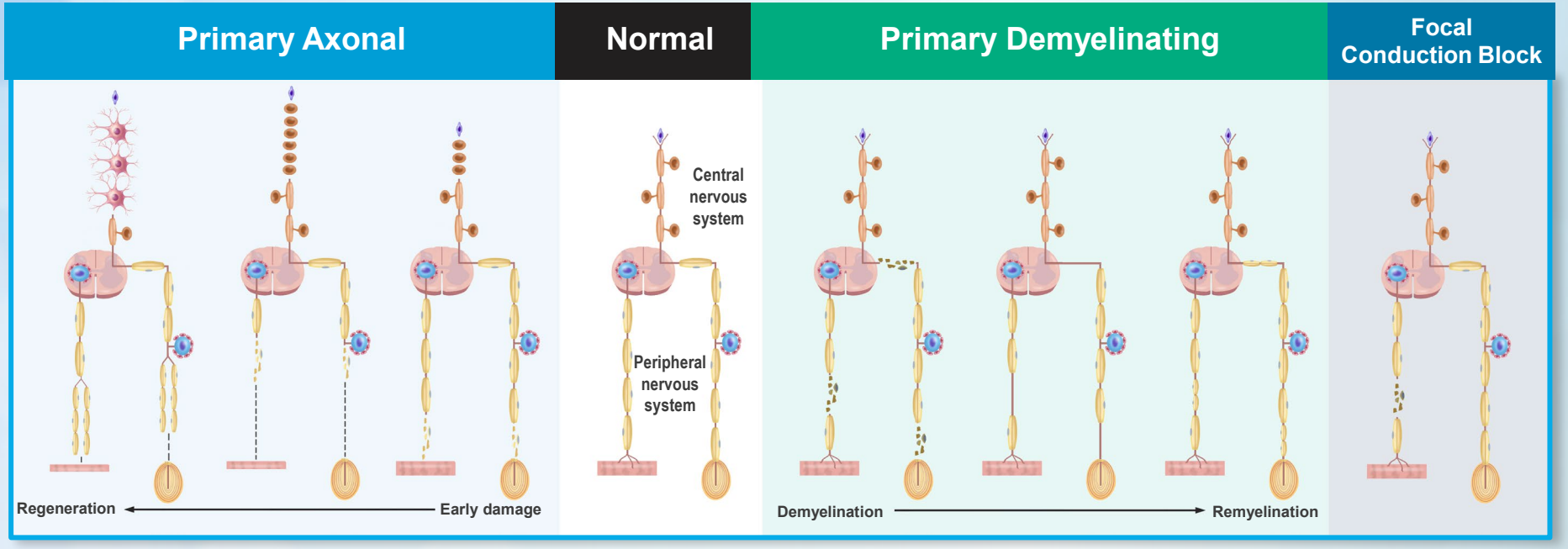

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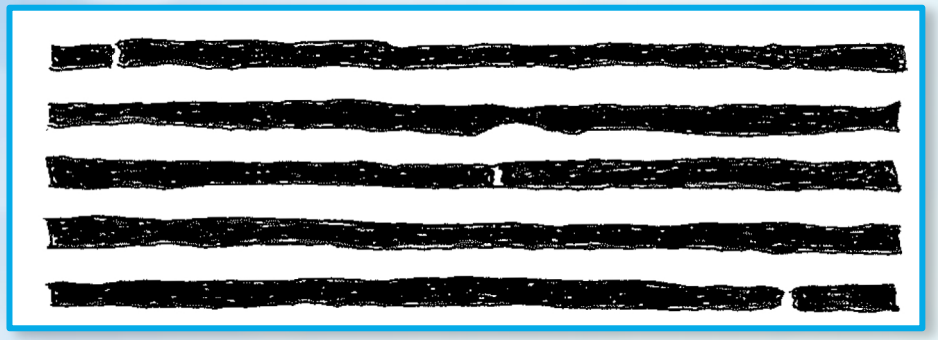
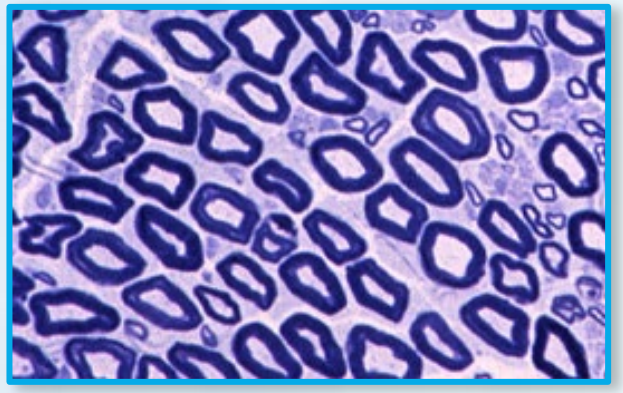
Pathology: Normal

- Teased fibers (sural nerve)



Uniform myelin thickness

- Cross section

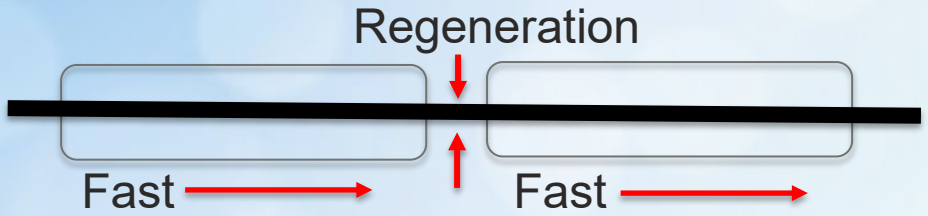


Uniform myelin profiles

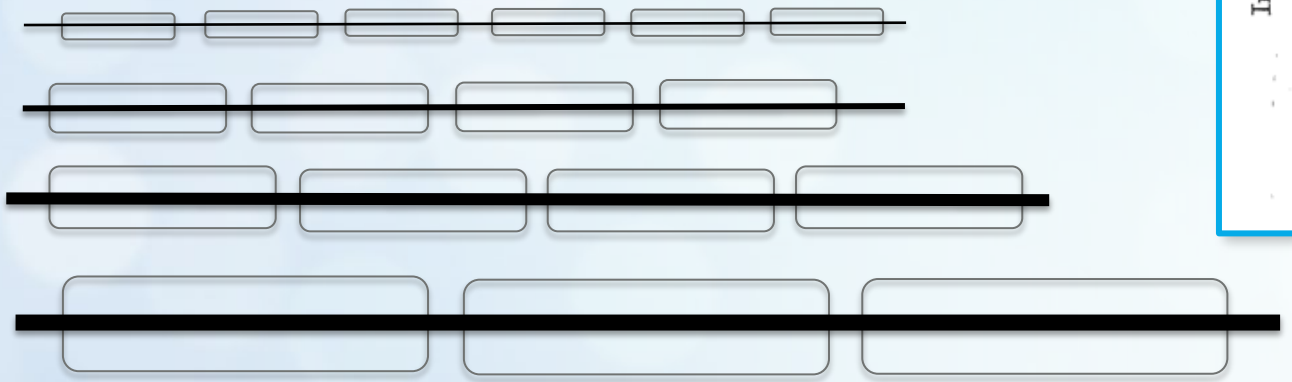
Teased fiber images courtesy of Mark Bromberg, MD, University of Utah, Salt Lake City, UT.
Cross-section image reprinted with permission of Alan Pestronk, MD, Washington University, St. Louis, MO.

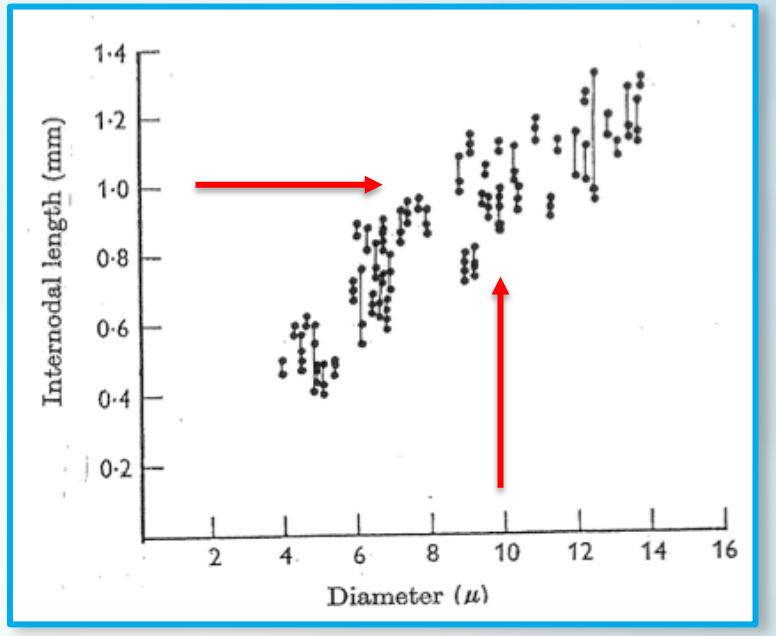
Physiology: Normal

- Saltatory conduction
  - Rapid along internode length
  - Regenerated at node of Ranvier



- Velocity proportional to fiber diameter
  - Larger fibers = longer internode length





Pathology: Demyelination

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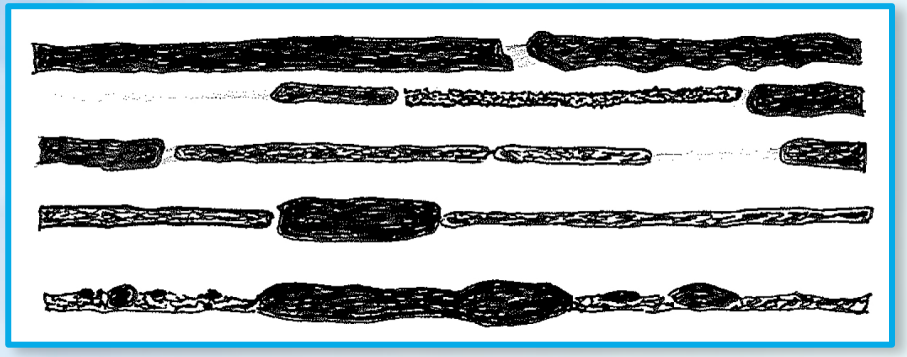
- Teased fibers (sural nerve)



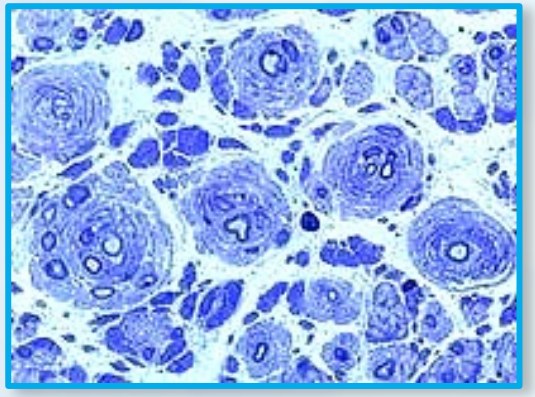
Demyelination paranodes/internodes

Irregular myelin

Large myelin ovoids

Myelin globules

- Cross section



Onion bulb formation

Demyelination/remyelination

Hereditary and acquired neuropathies

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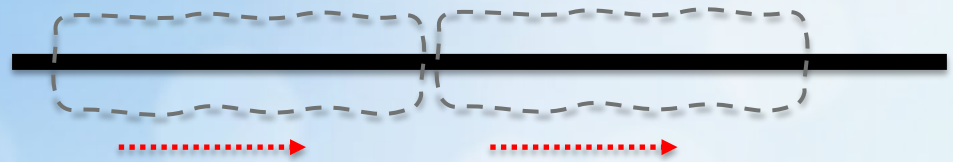
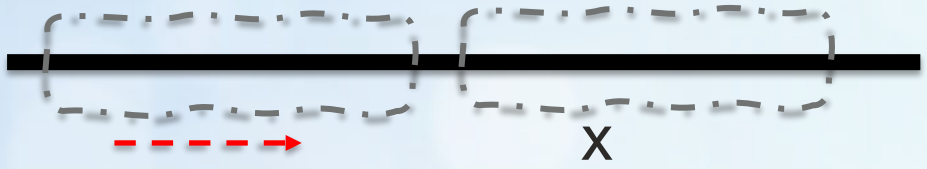
Physiology: Demyelination

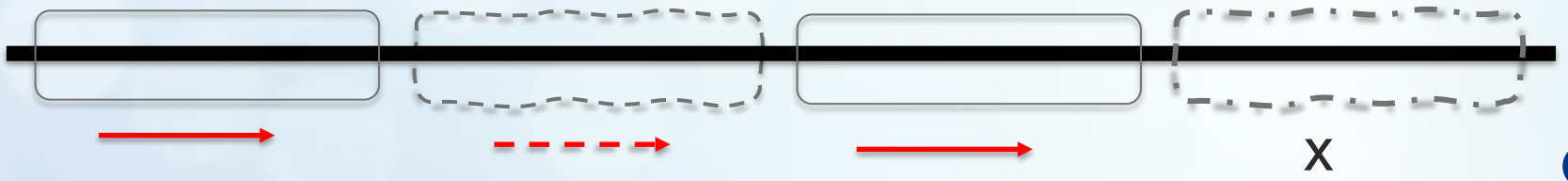
- Reduced myelin = current leakage



- Slow conduction or blocked conduction

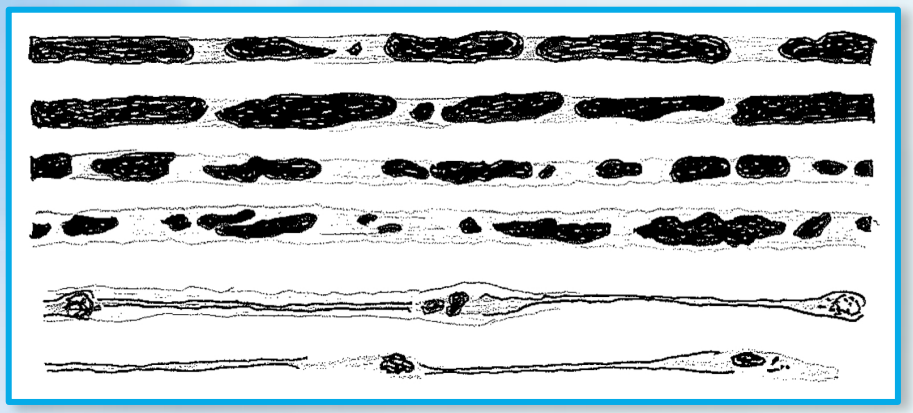


- At multiple sites along a nerve fiber



Pathology: Axonal

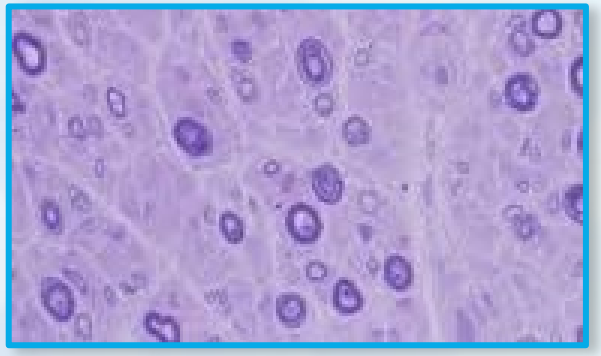
- Teased fibers (sural nerve)



Axonal degeneration

Axonal regeneration

- Cross section

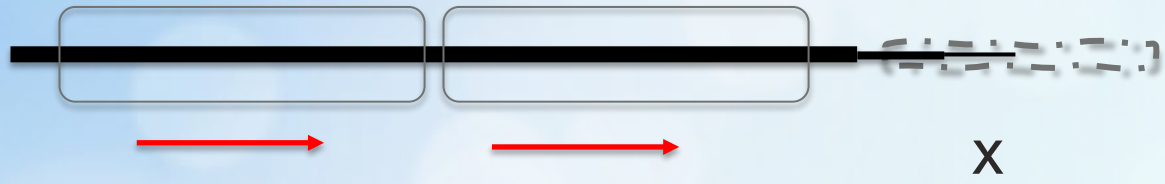


Sparse axons

Teased fiber images courtesy of Mark Bromberg, MD, University of Utah, Salt Lake City, UT.
Cross-section image reprinted with permission of Alan Pestronk, MD, Washington University, St. Louis, MO.

Physiology: Axonal Loss

- Loss of axon -> conduction stops



Pathology: Nodal Conduction Block

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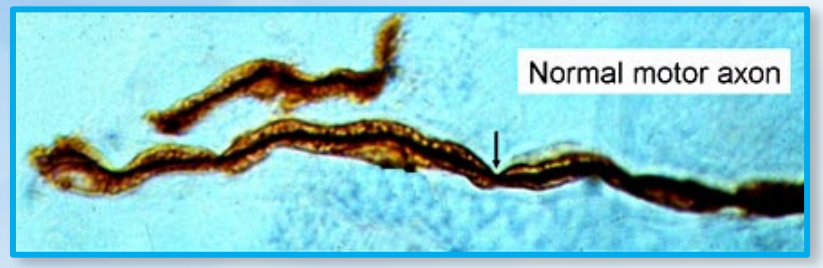
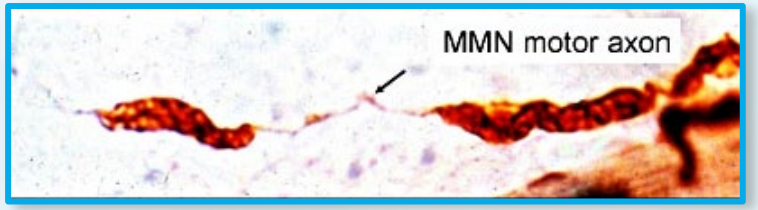
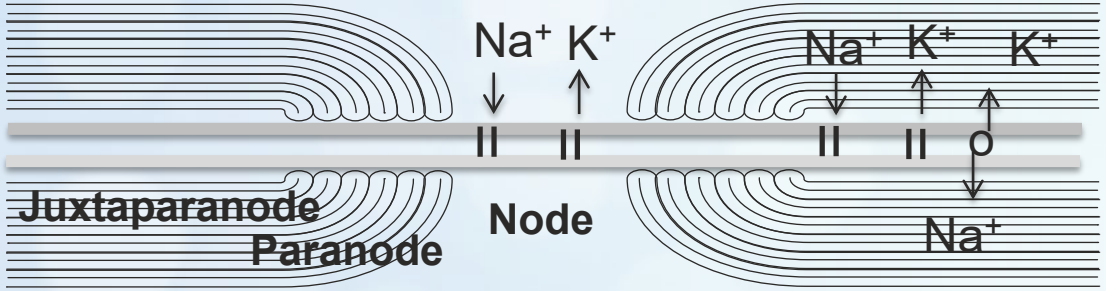
- Conduction block away from sites of entrapment
  - Teased fibers





  - May be no structural pathology
    - Nodopathy (channelopathy)



Antibody blockage

Altered channel function

Structural changes to myelin loops

Teased fibers images reprinted with permission of Alan Pestronk, MD, Washington University, St. Louis, MO.
Nodopathy image courtesy of Mark Bromberg, MD, University of Utah, Salt Lake City, UT.

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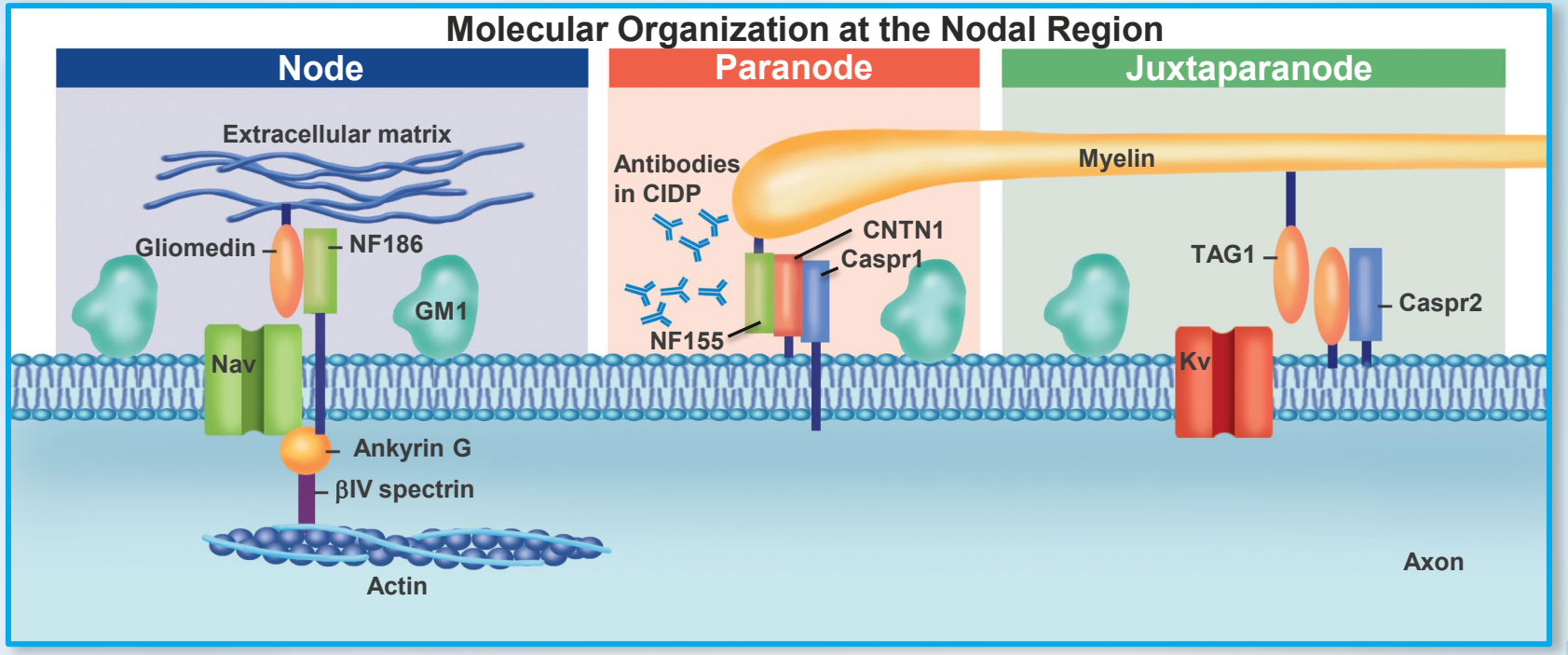
Nodal Pathology

- Antibody-mediated conduction block
  - Major factor in GBS[1]
  - Antibodies to NF155, CNTN1, and CASPR in CIDP[2,3]

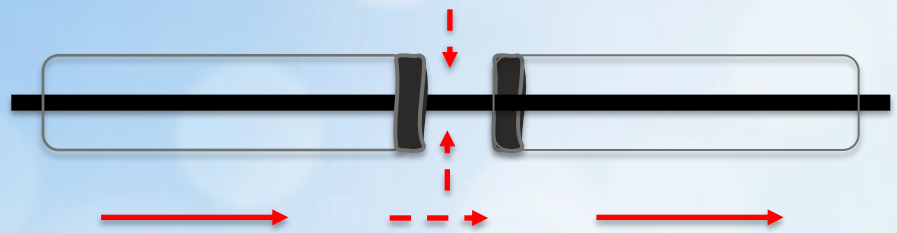


CASPR, contactin-associated protein 1; CNTN1, contactin-1; GBS, Guillain-Barré syndrome; NF, neurofascin; TAG-1, transient axonal glycoprotein 1.

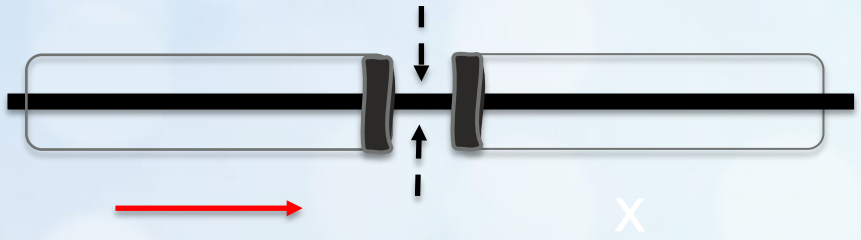
References: 1. van den Berg B. *Nat Rev Neurol.* 2014;10(8):469-482. **2.** Querol L. *Neurol Neuroimmunol Neuroinflamm.* 2015;2(5):e149. **3.** Vural A. *Front Immunol.* 2018;9:1029.

Physiology: Nodal Conduction Block

- Slowed regeneration; slowed conduction



- Blocked conduction



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CMAP: Normal Conduction

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Sensory vs Motor Nerves

- Sensory nerve action potential (SNAP) = amplitude in μV
  - Marked amplitude loss with axonal loss
    - Floor effect: Loss of ~65% of sensory nerve fibers ⇒ ∅ response
  - Marked amplitude loss over conduction distance
    - Segmental conduction velocity less useful
- Compound muscle action potential (CMAP) = amplitude in mV
  - Less amplitude loss with axonal loss
    - Can record response from 1 motor nerve fiber
  - Segmental conduction velocity and F-wave latency useful
- Most nerve conduction data based on motor fibers

Motor Nerve Conduction Metrics

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- CMAP amplitude or area ≈ number of axons
  - Caveat 1: collateral sprouting disguises degree of axonal loss
  - Caveat 2: abnormal temporal dispersion reduces CMAP

- CMAP timing ≈ integrity of myelin
  - Distal latency
  - F-wave latency
    - Chronodispersion (maximum – minimum latencies)[1]
  - Conduction velocity
    - Caveat: effects of loss of large nerve fibers
  - Negative peak duration

Timing from fastest conducting axon

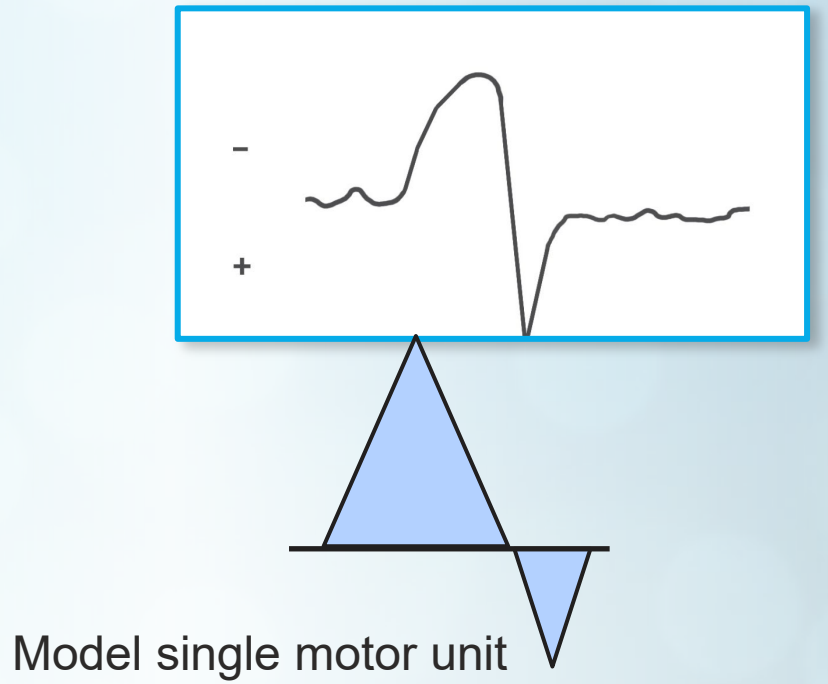
~Measure of slower conducting axons

CMAP, compound muscle action potential.

Reference: 1. Rajabally YA, Varanasi S. *Clin Neurophysiol*. 2013;124(1):171-175.

Single Motor Unit

- Single motor unit action potential
  - Biphasic potential (-/+)
  - ~4 ms −/~2 ms + duration = ~ 6-8 ms total duration
  - Different sizes/shapes
- Range of motor fiber CVs
  - 55 m/s – 40 m/s = normal temporal dispersion

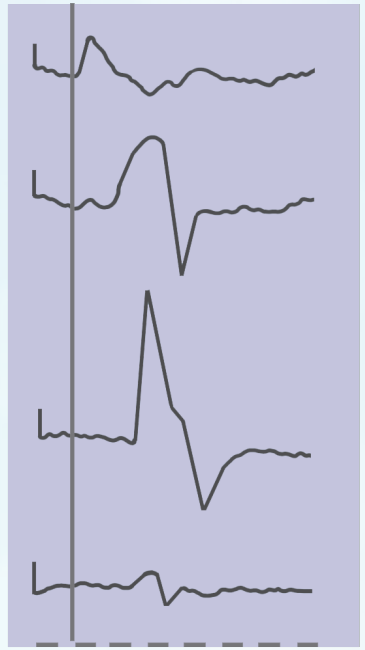


Model single motor unit

CV, conduction velocity.

CMAP: Result of Phase Cancellation

- CMAP = many single motor units
  - Different sizes, amplitudes, arrival times
  - Different juxtapositions of negative/positive phases

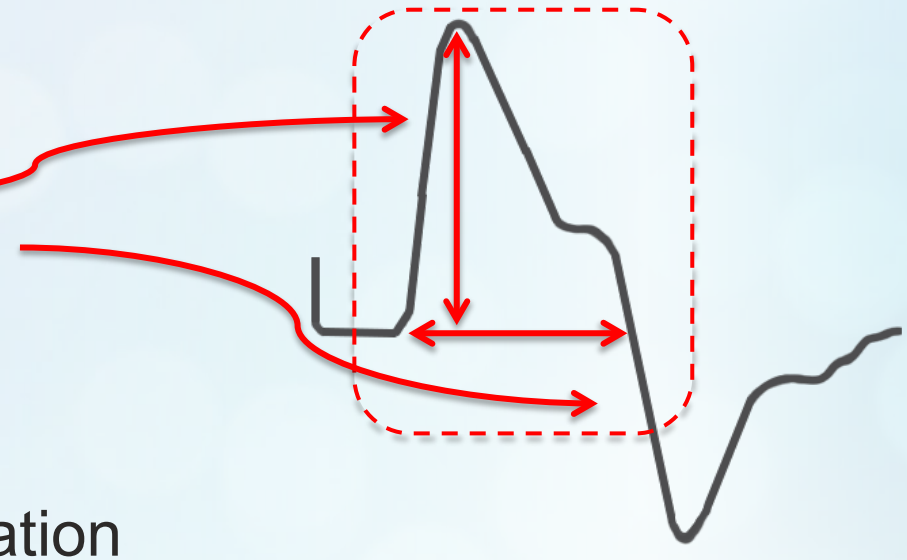


- CMAP = algebraic summation ⇒ 111 µV

CMAP, compound muscle action potential.

Viewing the CMAP

- CMAP
  - Negative peak amplitude
  - Negative peak duration
  - Steep rise time; smooth shape

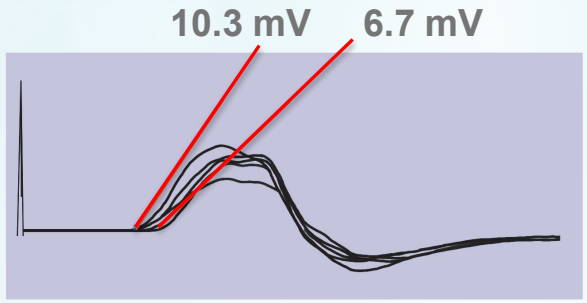


- Consider amplitude and duration <u>before</u> distal latency
  - Tables list distal latency first
  - Change table order!

CMAP, compound muscle action potential.

Caveat 1: CMAP Amplitude Variable

- Electrode (E1) position
  - Not based on anatomical landmarks
  - Move to find maximal amplitude CMAP (steeper negative slope)
  - Suggest sweep speed 2 ms/division to better observe slope steepness



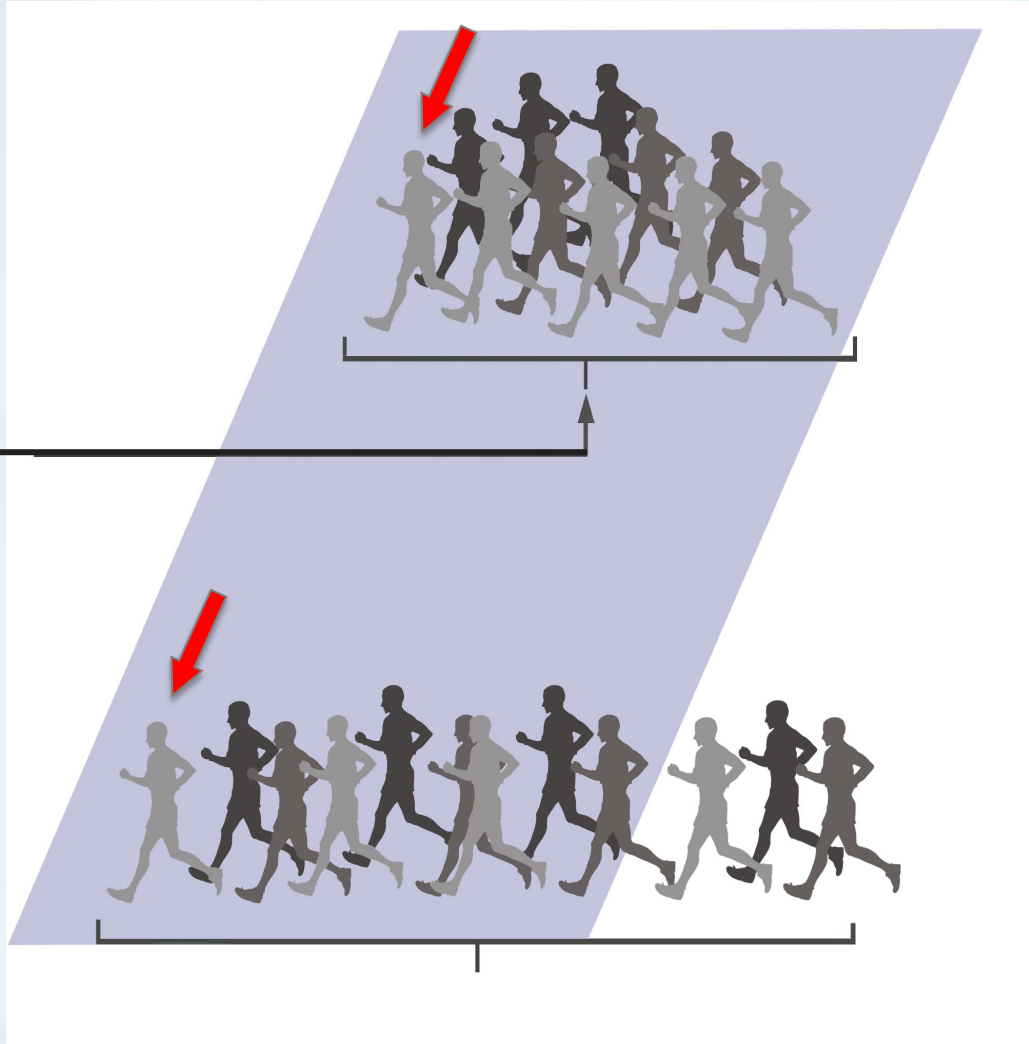
CMAP, compound muscle action potential.

Reference: Bromberg MB. *Electroencephalogr Clin Neurophysiol.* 1997;105(5):385-389.

Temporal Dispersion and Distance

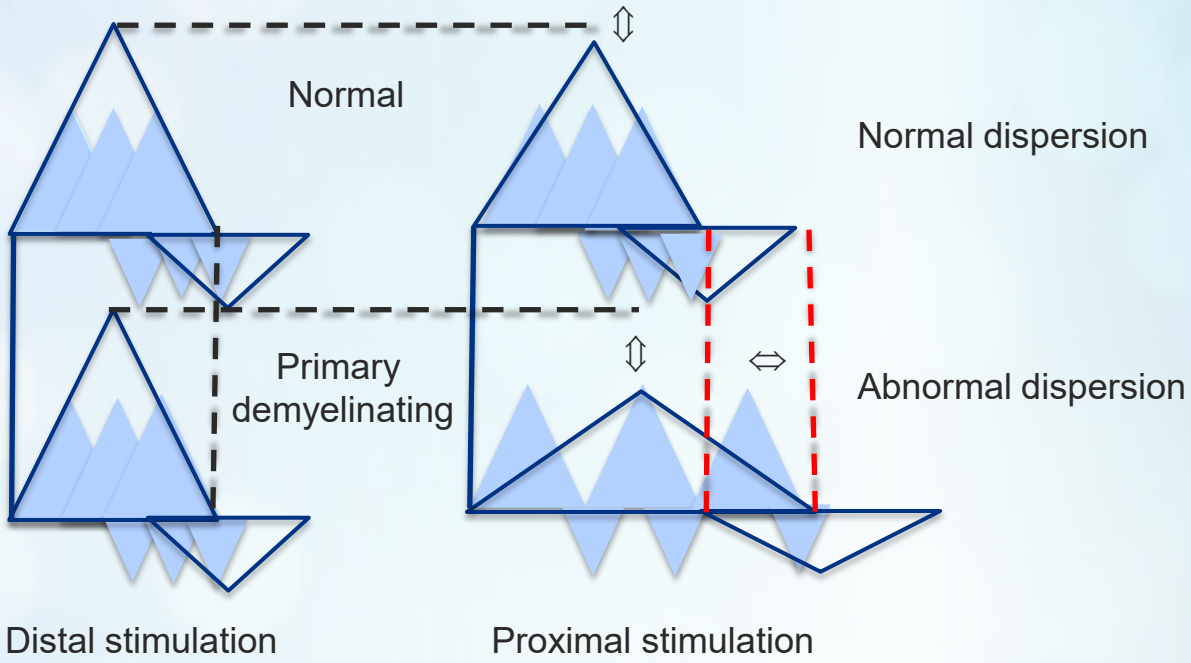
- Timing metrics
  - Fastest fiber(s)
  - Distal latency and conduction velocity
  - Slower fibers
  - Negative peak duration
  - Greater dispersion with greater distance

Runners: 6-7 min/mile
- 1 mile = 1 min
- 10 miles = 10 min



Model: Normal/Abnormal Temporal Dispersion and CMAP Amplitude

- Effect of slower fiber conduction: ⇓ amplitude and ⇑ negative peak duration



CMAP, compound muscle action potential.

Phase Cancellation and Normal Temporal Dispersion

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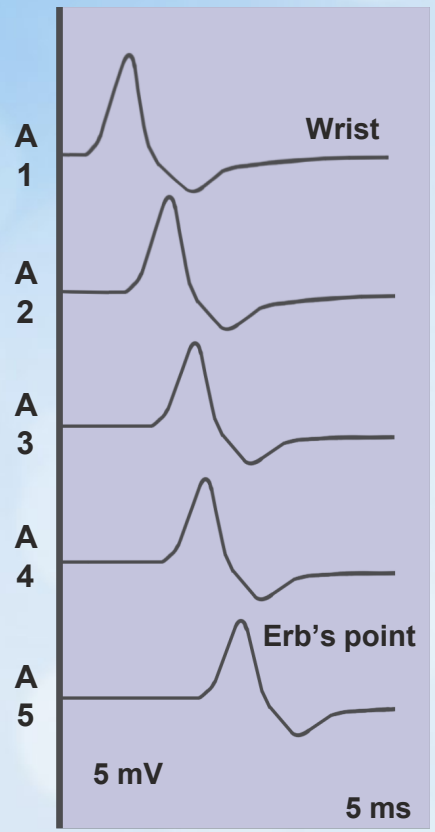
Phase cancellation

⇓ Amplitude > ⇓ area



Normal phase cancellation (wrist to Erb's point)

⇓ 19% area/ ⇓ 21% amplitude
⇑ 11% negative peak duration

Cannot have proximal amplitude > distal amplitude

Reference: Bromberg MB. *J Clin Neuromuscul Dis*. 2015;16(3):141-152.

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CMAP: Axonal Loss

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How Many Axons?

- Cannot “count” motor fibers
  - Anatomical counts ≅ Motor Unit Number Estimation (MUNE) values

Muscle	Number of motor units: MUNE	Number of motor units: anatomical estimates
First dorsal interosseous	144 ± 4	119
Thenar	276 ± 35	171 ± 30
Hypothenar	285 ± 103	130 ± 15
Extensor digitorum brevis	290 ± 71	

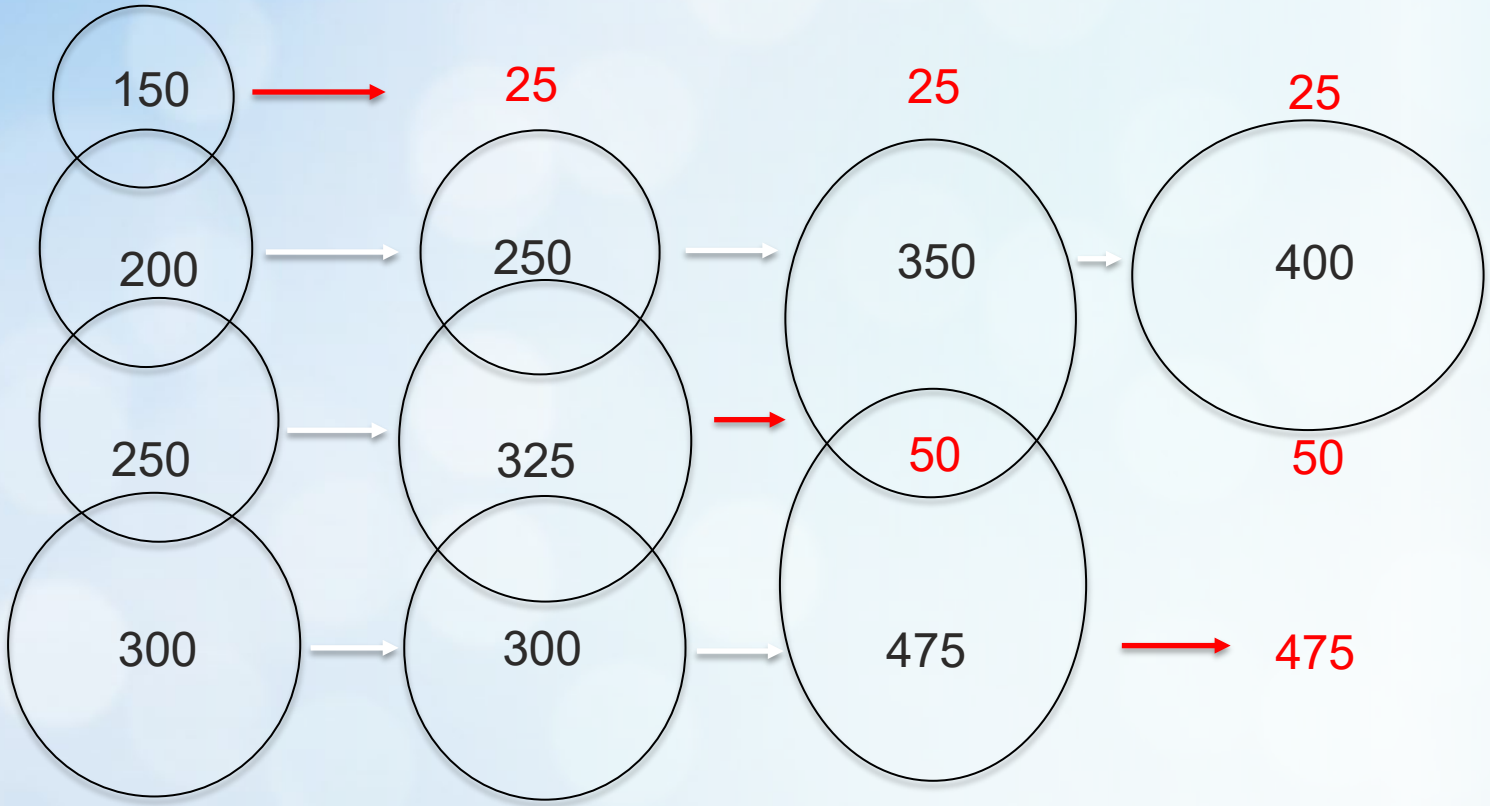
  - About 200 fibers in commonly studied nerve-muscles

M B Bromberg, MN 61:131-142 (2020)

Axonal Loss: Collateral Reinnervation

- Progressive axonal loss

Number of muscle fibers in MU/MU territory



Collateral Reinnervation: Effect on Metrics

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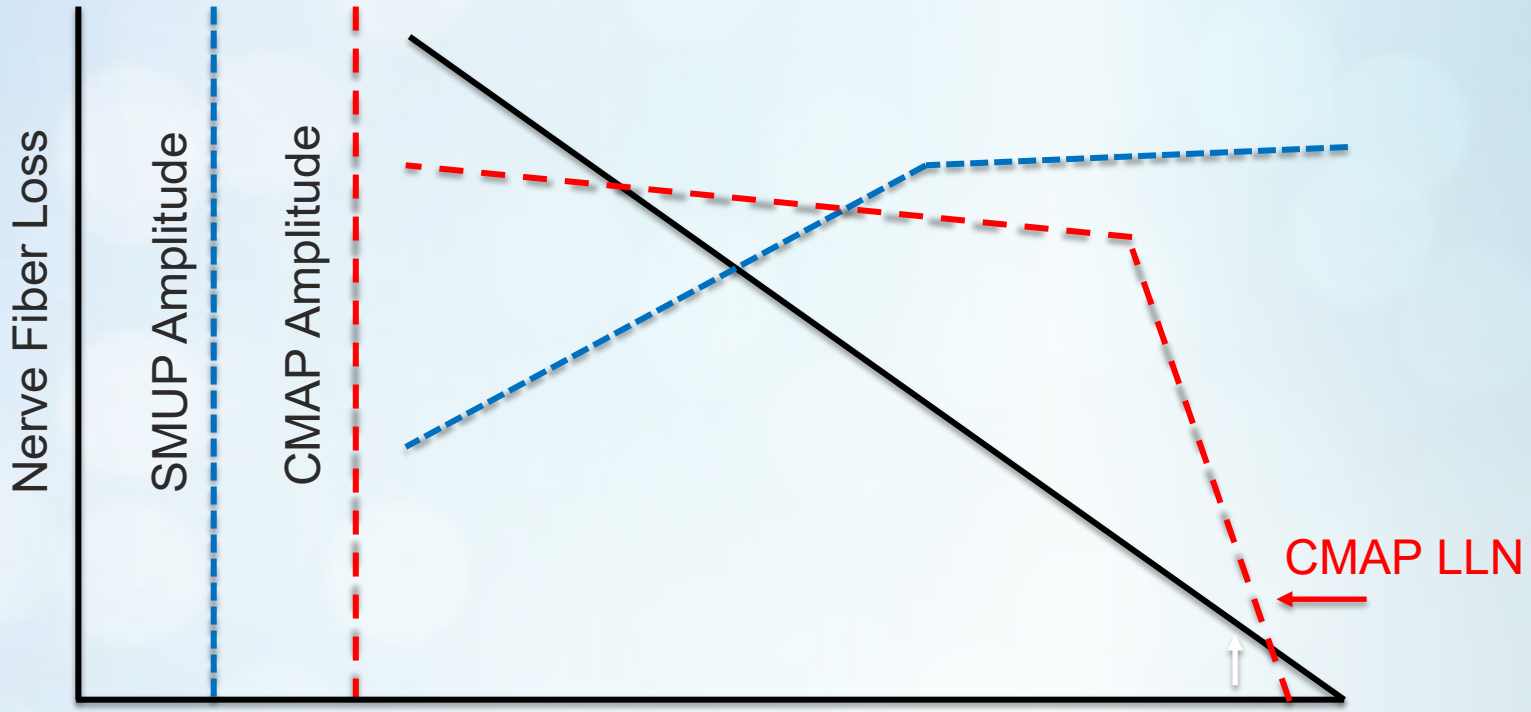
- Progressive nerve fiber loss



SMUP: Single motor unit potential CMAP: Compound muscle action potential LLN: Lower Limit of Normal

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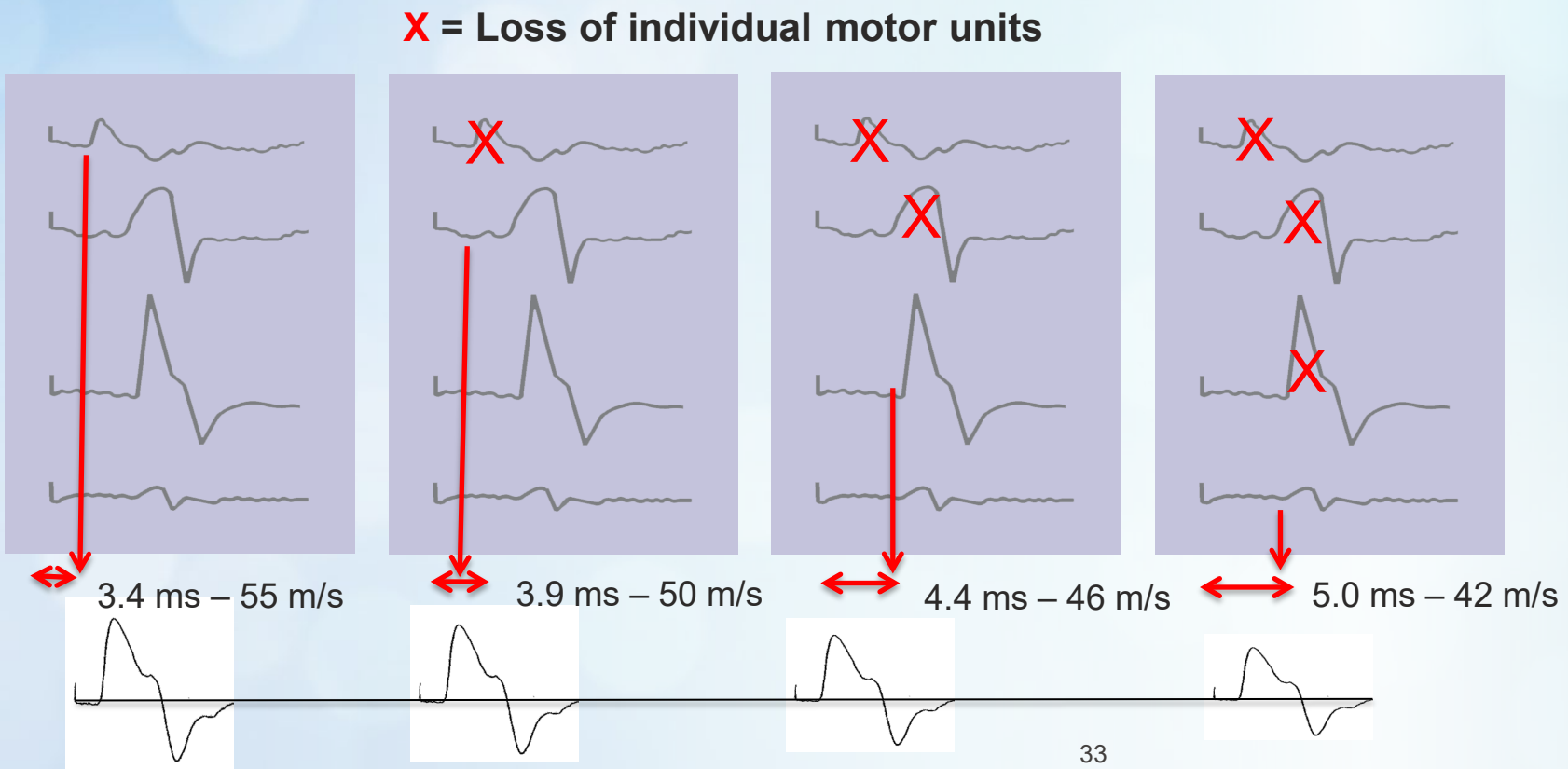
Axonal Loss and Timing Metrics

- Loss of fastest fibers: ⇓ conduction velocity; ⇑ distal latency and F-wave latency
  - Range of motor fiber CVs: 55 m/s – 40 m/s



Large Motor Fiber Loss in CIDP

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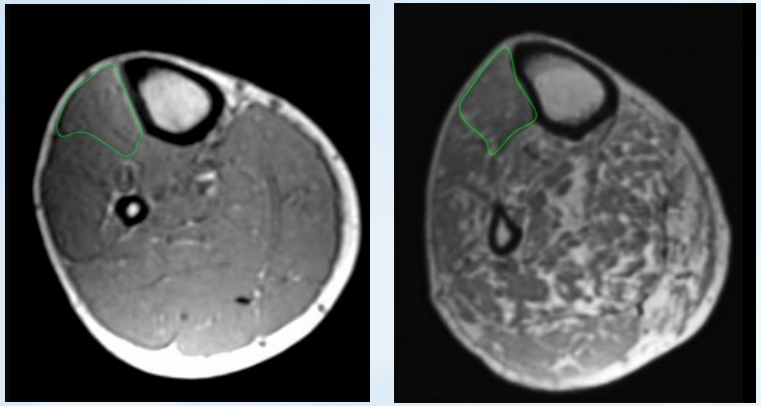
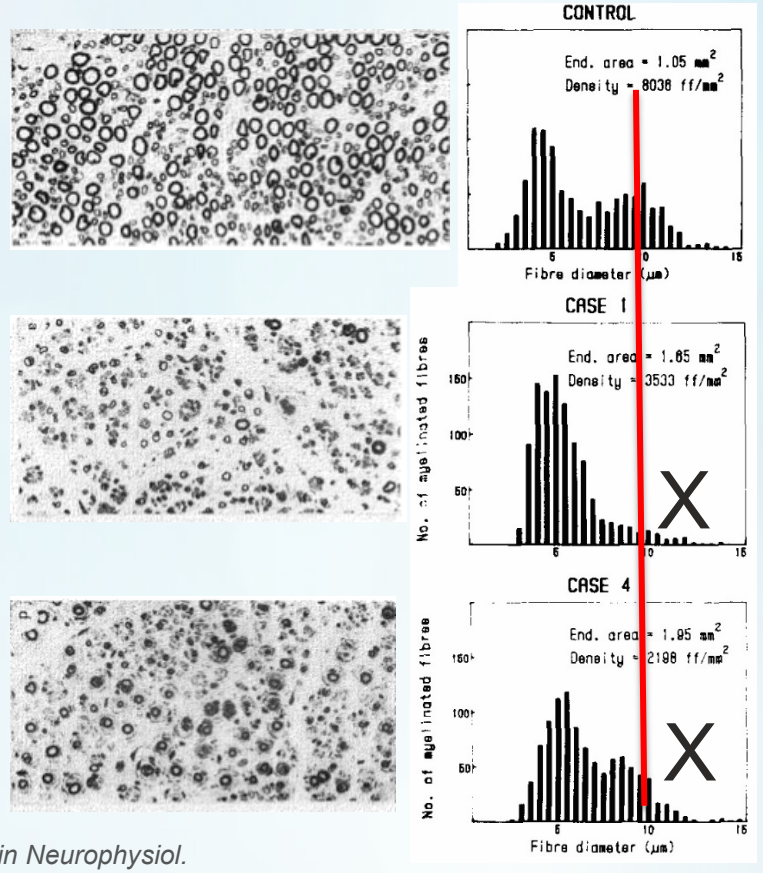
- Motor Unit Number Estimaton[1,2]
  Anterior tibialis: ⇓ 27%1
- Motor potential metrics
  Amplitude: ⇑ 32%[1]
  Jitter: ⇑ 44% = neuromuscular junction instability[1]
- Magnetic Resonance Imaging[3]



CIDP Sural Nerve[4]



References: 1. Gilmore KJ. *Muscle Nerve.* 2017:56(3):413-420. **2.** Paramanathan S. *Clin Neurophysiol.* 2016:127(1):898-904. **3.** Gilmore KJ. *Muscle Nerve.* 2018;58(3):396-401. **4.** Barbieri F. *Clin Neurol Neurosurg.* 1991;93(2):99-106. Left image from Kawamura Y. *J Neuropathol Exp Neurol.* 1981;40(6):667-675, by permission of the American Association of Neuropathologists, Inc; right image from Barbieri F. *Clin Neurol Neurosurg.* 1991;93(2):99-106, copyright 1991, with permission from Elsevier.

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CMAP: Multifocal Demyelination

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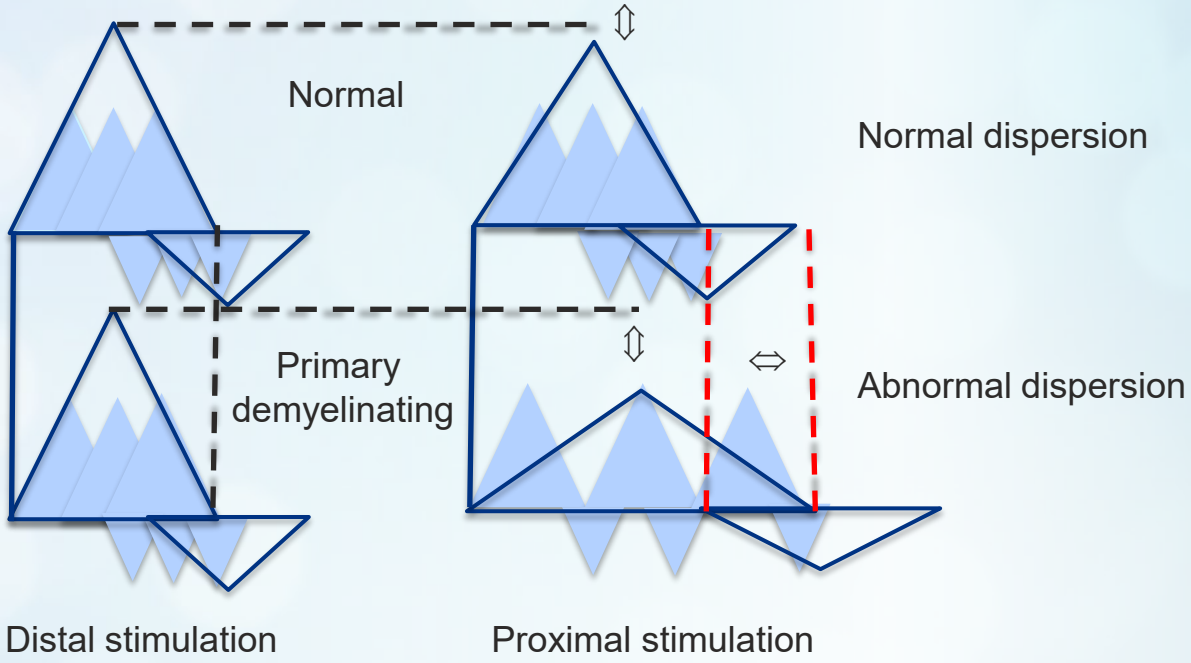
Multifocal Demyelination: Nerve Conduction Findings

- Slow conduction along fibers
  - Abnormal temporal dispersion
    - Increased negative peak duration
  - Greater phase cancellation
    - Reduced proximal CMAP amplitude/area
    - Effects of ⇓ amplitude and ⇑ negative peak duration greater over longer conduction distances
  - Sites for pathology
    - Large fibers: 1 mm internode = 3000 segments in leg nerves
    - More sites for smaller nerves
      - Ulnar nerve with stimulation wrist-axilla to maximize detection of abnormal temporal dispersion

CMAP, compound muscle action potential.

Model: Temporal Dispersion and CMAP Amplitude

- Slower fiber conduction: ⇓ amplitude and ⇑ negative peak duration



CMAP, compound muscle action potential.

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CMAP: Conduction Block

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Conduction Block: Focal

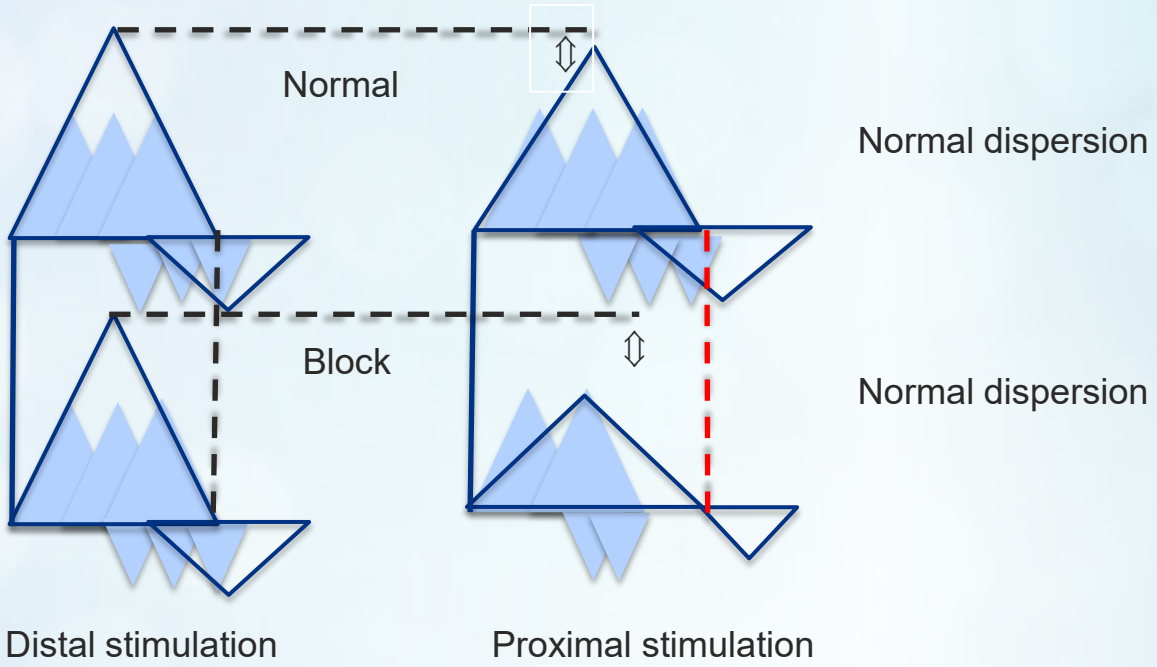
- Focal conduction block
  - Normal temporal dispersion
    - Minimal change in negative peak duration
  - Normal phase cancellation
    - Reduced proximal CMAP area/amplitude due to loss of blocked fibers
    - Criteria:

	CMAP Amplitude	CMAP Area	CMAP Negative Peak Duration
Definite Block	⇓ ≥ 50%	⇓ >40%	⇑ ≤ 30%
Probable Block	⇓ ≥ 30%	⇓ >30%	⇑ ≤ 30%

CMAP, compound muscle action potential.
Reference: Olney et al. MN (2003)

Focal Conduction Block

- Normal fiber conduction: ⇓ amplitude and minimal change negative peak duration



CMAP, compound muscle action potential.

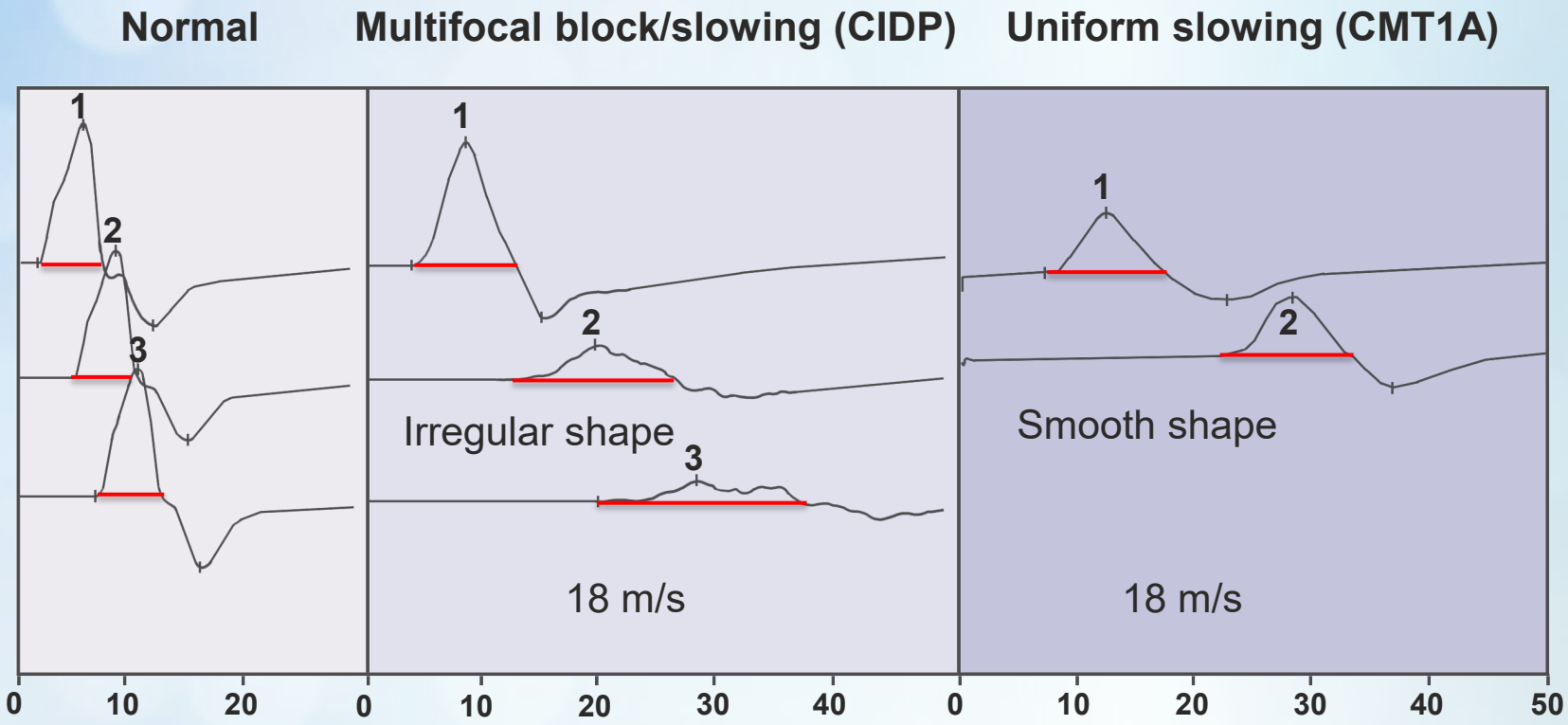
CIDP: Multifocal Demyelination + Block + Axonal Loss

- Multifocal along nerve
  - Demyelination
    - Slowing
    - Conduction block
  - Nodopathy
    - Slowing
    - Conduction block
  - Secondary axonal loss

- Difficult to distinguish pure conduction block from abnormal temporal dispersion
  - Term: “Abnormal temporal dispersion/conduction block”

CMAP, compound muscle action potential.

Multifocal Slowing/Block vs Uniform Slowing



CMT1A, Charcot-Marie-Tooth disease type 1A.

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Diagnostic Criteria

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Criteria for Primary Demyelination

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- Consensus (expert opinion) and modeling (animal or human motor unit waveforms)
- Criteria based on[1]
  - Slowing: DL, CV, F-WL, TD
  - Number of abnormalities
  - Number of nerves involved
- Tested on patients with clinical CIDP diagnosis
  - Criteria revised and retested, revised and retested…
  - 16+ sets of criteria[1]
  - Sensitivity applied to “CIDP” patients = 11%-95%[1]

CV, conduction velocity; DL, distal latency; F-WL, F-wave latency; TD, temporal dispersion.

Reference: 1. Bromberg MB. *Muscle Nerve.* 2011;43(6):780-794.

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Axonal Loss vs Timing Metrics

- How much change in CMAP metrics accounted for by axonal loss?
- Amyotrophic lateral sclerosis (ALS) example of pure axonal loss: metrics[1]
  - CV >75% of LLN
  - Distal latency <125% of ULN
  - F-wave latency <125% of ULN
- If percentages exceed these limits, must include element of demyelination

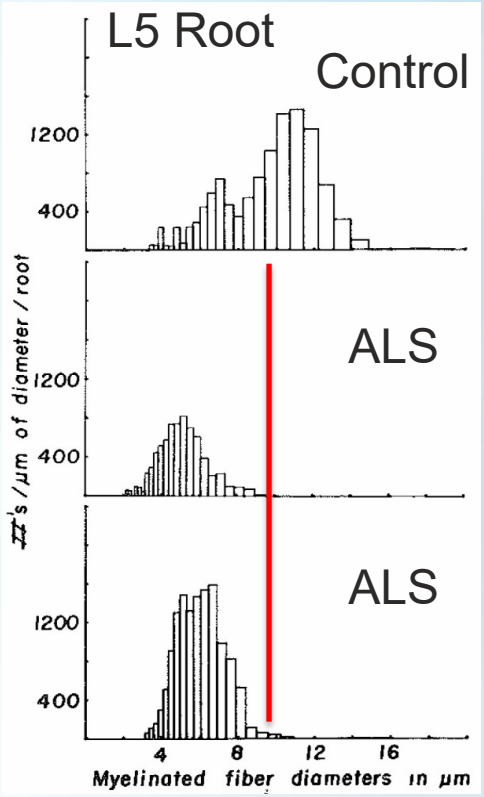

Figure: Dyck PJ, ed. *Peripheral Neuropathy.* Vol. 1. 3rd ed. Philadelphia, PA: WB Saunders; 1993.

CMAP, compound muscle action potential; LLN, lower limit of normal; ULN, upper limit of normal.

Reference: 1. Cornblath DR. *Muscle Nerve.* 1992;15(10):1111-1115.

EAN/PNS Revised CIDP Criteria

- Typical CIDP
- CIDP variants
  - Distal CIDP (distal acquired demyelinating symmetric neuropathy [DADS])
  - Multifocal CIDP
    - Multifocal demyelinating neuropathy with persistent conduction block
    - Lewis-Sumner syndrome (LLS)
    - Multifocal acquired demyelinating sensory and motor neuropathy (MADSAM)
    - Multifocal inflammatory demyelinating neuropathy (MIDN)
  - Focal CIDP
  - Motor CIDP
  - Sensory CIDP
- Not classified as CIDP
  - Chronic immune sensory polyradiculopathy (CISP)
  - Autoimmune nodopathies

EAN, European Academy of Neurology; PNS, Peripheral Nerve Society.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268. .

EAN/PNS Revised CIDP Electrodiagnostic Criteria

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- Motor nerves
  - Strongly supportive of demyelination: abnormality in ≥2 nerves

Distal latency	≥150% of ULN in ≥2 nerves (excluding median wrist)
Conduction velocity	≤70% of LLN in ≥2 nerves
F-wave latency	≥120% of ULN in ≥2 nerves if distal CMAP ≥80% of LLN ≥150% of ULN in ≥2 nerves if distal CMAP <80% of LLN
Absent F-wave	≥2 nerves if distal CMAP ≥120% of LLN + ≥1 abnormality in ≥1 nerves
Conduction block	>30% reduction proximal CMAP amplitude if distal CMAP ≥120% of LLN in ≥2 nerves (excluding tibial nerve) OR ≥1 nerve + ≥1 demyelinating feature (except absent F-wave)
Abnormal dispersion	>130% proximal:distal negative peak CMAP duration/≥100% in tibial nerve in ≥2 nerves
Distal CMAP duration (2 Hz low frequency filter)	>8.4 ms median, >9.6 ms ulnar, >8.8 ms peroneal, >9.2 ms tibial in ≥1 nerve + ≥1 other demyelinating feature in ≥1 other nerve

- No longer “definite” or “probable” CIDP
  - Weakly supportive of demyelination: in only 1 nerve

EAN, European Academy of Neurology; LLN, lower limit of normal; PNS, Peripheral Nerve Society; ULN, upper limit of normal.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268.

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EAN/PNS Revised Criteria

- Sensory nerves
  - Strongly supportive: 2 abnormalities in sensory nerves
    - Distal latency > ULN
    - SNAP amplitude < LLN
    - Conduction velocity < LLN

Conduction Velocity	<80% of LLN if SNAP amplitude >80% LLN in ≥2 nerves <70% of LLN if SNAP amplitude <80% LLN in ≥2 nerves

  - Weakly supportive: 1 abnormality
- Sensory CIDP
  - Abnormal sensory nerve study
  - Normal motor nerve conduction studies

EAN, European Academy of Neurology; LLN, lower limit of normal; PNS, Peripheral Nerve Society; ULN, upper limit of normal.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268.

EAN/PNS Revised Criteria Notes

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- Bandpass filters: 2 Hz-10 kHz
- Skin temperature: ≥33°C palm; ≥30°C foot
- Nerves studied
  - Median, ulnar (below elbow), peroneal (below fibular head), tibial one side
  - Contralateral nerves or ulnar + median at axilla and Erb's point
    - ≥50% CMAP amplitude loss Erb's point-wrist for ulnar + median
  - Slowing ulnar across elbow/peroneal across fibular head not applicable
- Issues
  - If distal CMAP <1 mV, record from more proximal muscles
  - If ulnar conduction block, exclude Martin-Gruber anastomosis
  - If median conduction block, exclude distal costimulation of ulnar nerve

CMAP, compound muscle action potential; EAN, European Academy of Neurology; PNS, Peripheral Nerve Society.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268.

EAN/PNS Revised CIDP Electrodiagnostic Criteria

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- Typical CIDP
  - Abnormalities in ≥2 motor nerves + ≥2 sensory nerves; in 1 nerve = "possible typical CIDP"
- Distal CIDP (DADS)
  - Abnormalities in ≥2 upper limb motor nerves + ≥2 sensory nerves; in 1 nerve = "possible distal CIDP"
- Multifocal CIDP (LSS/MADSAM)
  - Abnormalities in ≥2 motor nerves in >1 limb + ≥2 sensory nerves in affected limbs
- Focal CIDP
  - Abnormalities in ≥2 motor nerves in 1 limb + ≥2 sensory nerves in affected limbs
- Motor CIDP
  - Abnormalities in ≥2 motor nerves + normal sensory nerves 4 nerves
- Sensory CIDP
  - Normal motor nerves 4 nerves + abnormalities in ≥2 sensory nerves = "possible sensory CIDP"

DADS, distal acquired demyelinating symmetric neuropathy; EAN, European Academy of Neurology; LSS, Lewis-Sumner syndrome; MADSAM, multifocal acquired demyelinating sensory and motor neuropathy; PNS, Peripheral Nerve Society.

Reference: van den Bergh PYK. *J Peripher Nerv Syst*. 2021;26(3):242-268.

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EFN/PNS Criteria: Sensitivity and Specificity

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- 120 CIDP patients
  - Clinical features
  - Treatment response
    - ≥1 point Overall Neuropathy Limitation Scale
    - ≥4 points Inflammatory Rasch-Built Overall Disability scale
    - ≥5 kg increase grip

vs

- 100 non-CIDP patients
  - Clinical features
  - Excluded CMT patients

- EFN/PNS (motor nerves)

Sensitivity	Specificity
~92% typical, ~98% typical + possible CIDP	94% typical, 79% possible

- EFN/PNS (sensory nerves)

Sensitivity	Specificity
93% typical	60%

- False positive issues
  - Distributed amongst nerves and metrics

Reference: Rajabaly YA. JNNP 93:1247-1252 (2022)

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Diagnostic Challenges

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Criteria Challenges: Simplified Guidelines

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- EFN/PNS criteria challenging to follow
- Consider ALS-based limits as a guideline
- Calculate lab's 75%/125% values

	DL ULN	DL >125% ULN	F-WL ULN	F-WL >125% ULN	CV LLN	CV <75% LLN
Median	4.4	>5.5	31	>38.8	49	**<37**
Ulnar	3.5	>4.4	31	>38.8	49	**<37**
Fibular	6.1	>7.6	55	>68.8	41	**<31**
Tibial	6.1	>7.6	55	>68.8	41	**<31**

- Negative peak duration (~6.0-8.0 ms) >125% (>9.0 ms)

CV, conduction velocity; DL, distal latency; F-WL, F-wave latency; LLN, lower limit of normal; ULN, upper limit of normal.

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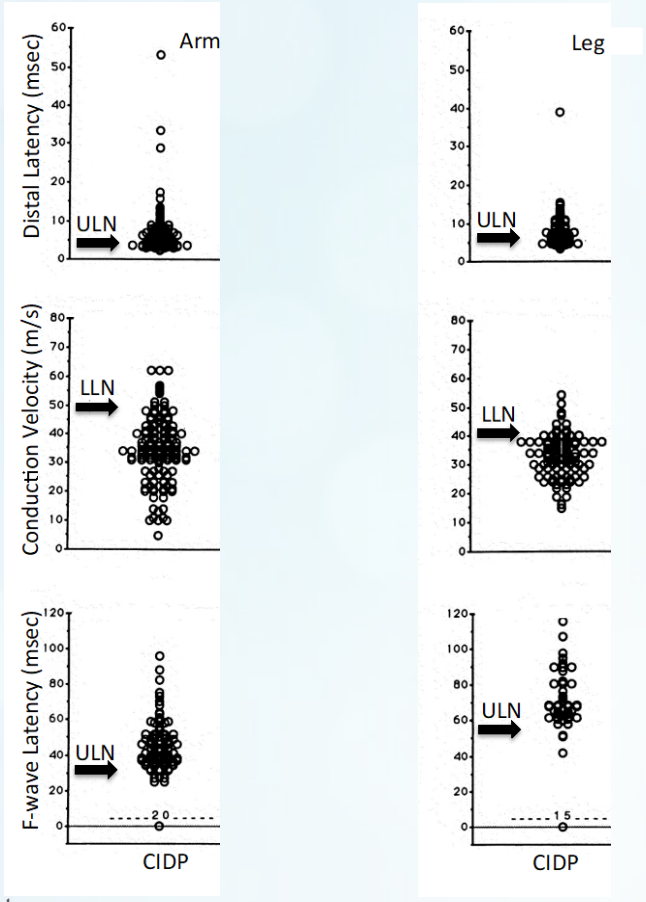
Nerve Conduction Challenges

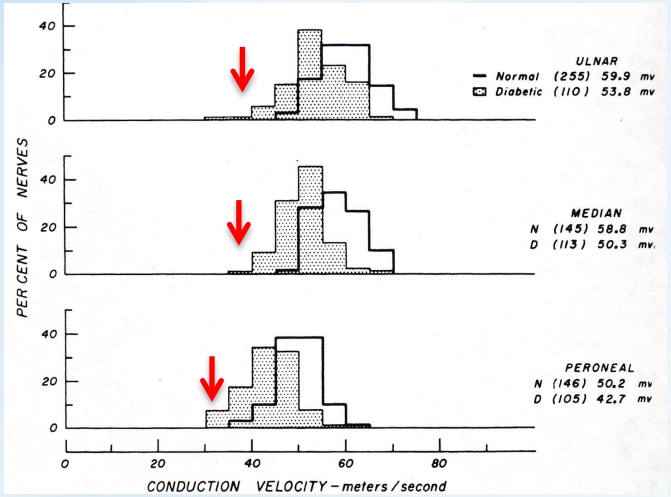
- Not all nerves affected: CIDP values overlap with normal values

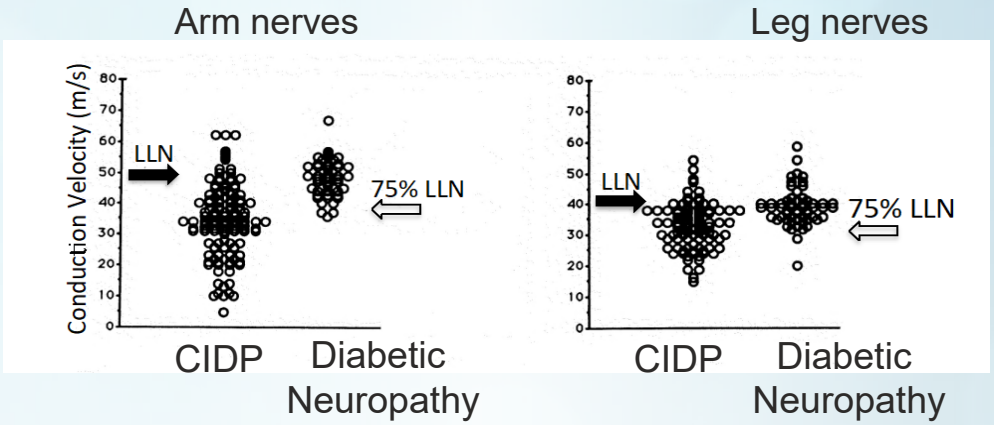


Reference: Bromberg MB. *Muscle Nerve.* 1991;14(10):968-976. Image copyright 1991 John Wiley & Sons, Inc., reprinted with permission.

CIDP vs Diabetic Neuropathy

- Mild slowing with diabetes[1,2]
  - Timing metrics overlap
- CIDP more common with diabetes?[3]
  - Reports +/-





References: 1. Mulder DW. *Neurology.* 1961;11(4 pt 1):275-284. **2.** Bromberg MB. *Muscle Nerve*. 1991;14(10):968-976. **3.** Bril V. *J Diabetes Complications.* 2016;30(7):1401-1407. Left image from Mulder DW. *Neurology.* 1961;11(4 pt 1):275-284 (http://www.neurology.org/), reprinted with permission from Wolters Kluwer Health, Inc.; right image from Bromberg MB. *Muscle Nerve*. 1991;14(10):968-976, copyright 1991 John Wiley & Sons, Inc., reprinted with permission.

Diagnostic Errors: Other Neuropathies

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- ALS
  - Overinterpretation of mild degree of slowing from axonal loss
  - Not sure why diagnosed as CIDP
    - Felt to be MMN?
- Idiopathic neuropathy
  - Overinterpretation of mild degree of slowing from axonal loss
  - Likely axonal neuropathy
- Hereditary neuropathy
  - Did not consider family history
  - Varying degrees of slowing
    - CMT1A: <38 m/s in arm nerve

ALS, amyotrophic lateral sclerosis; CMT1A, Charcot-Marie-Tooth disease type 1A; MMN, multifocal motor neuropathy.

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Technical Issues

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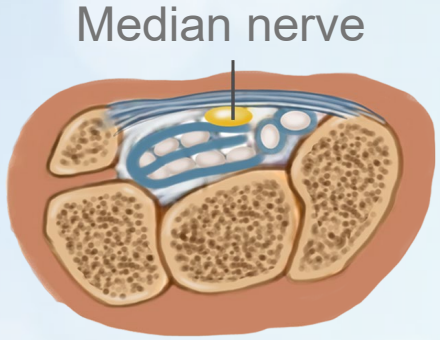
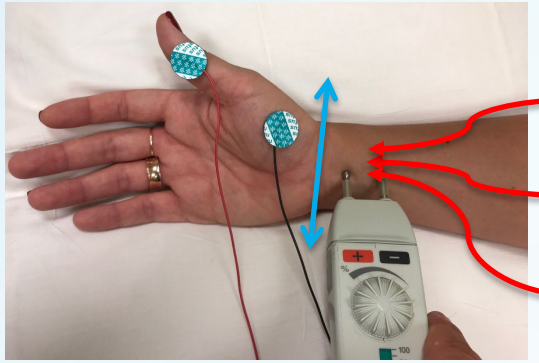
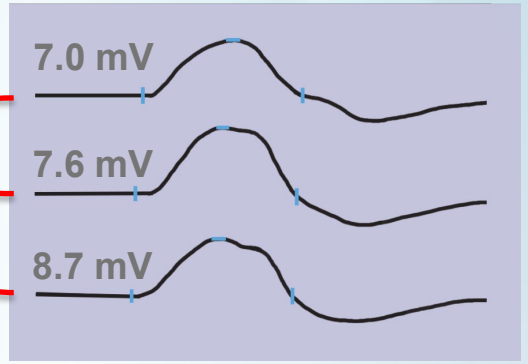
Nerve Stimulation

- Determine optimal stimulation site over nerve
  - Supramaximal (but not superduper maximal) stimulation
    - Overstimulation can activate neighboring nerves







Photograph courtesy of Mark Bromberg, MD, University of Utah, Salt Lake City, UT.

Reference: Bromberg MB. *J Clin Neuromuscul Dis*. 2015;16(3):141-152.

Sensory Nerve Patterns for AIDP/CIDP

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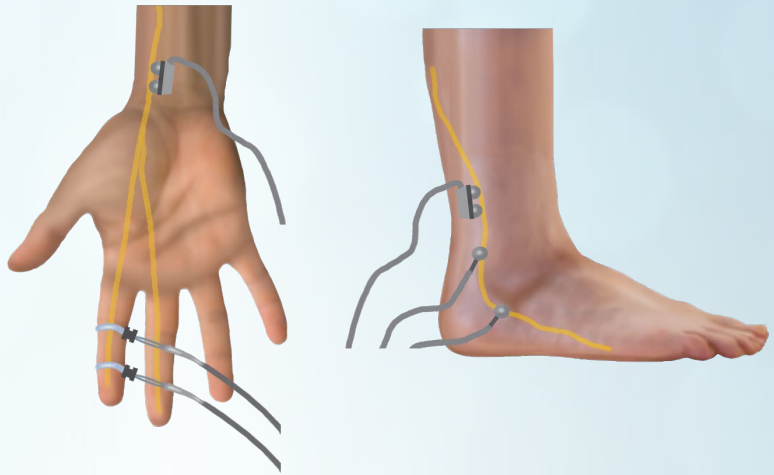
- Responses may be absent
- Abnormal median/normal sural (radial)

Abnormal median/ normal sural	39%	28%	14%-23%
Absent median/ present sural	19%	16%	0%
Normal median/ abnormal sural	3%	7%	10%-18%
Present median/ absent sural	3%	23%	13%-45%



AIDP, acute inflammatory demyelinating polyradiculoneuropathy; DPN, diabetic polyneuropathy.

Reference: Bromberg MB. *Muscle Nerve.* 1993;16(3):262-266.

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Very Distal Demyelination/Conduction Block

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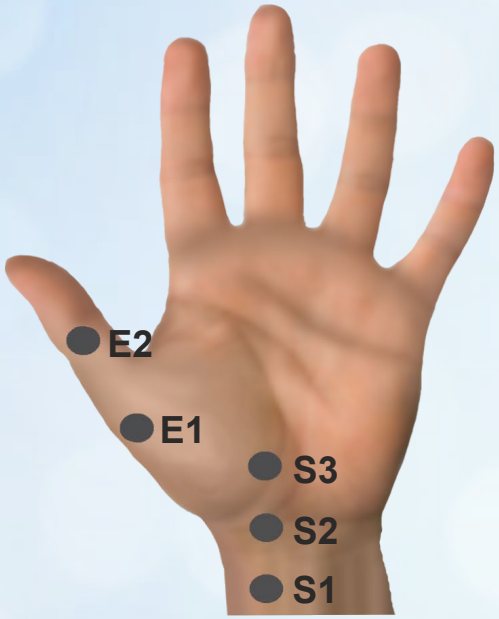
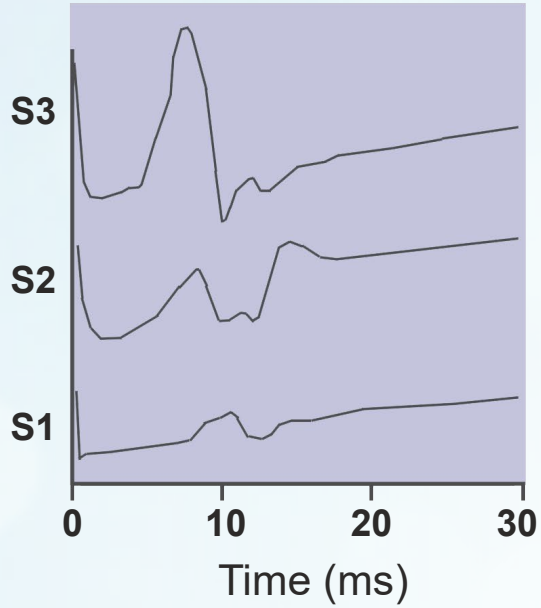
- Assess for greater CMAP amplitude at more distal stimulation sites (very distal conduction block)





Standard stimulation distance = S1

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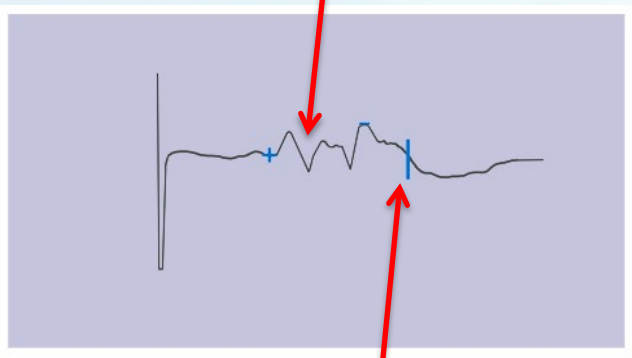
CMAP, compound muscle action potential.

Duration Markers

- Duration markers dependent upon low frequency filter: usually 20 Hz
- Duration markers may be misplaced with very prolonged and complex CMAP waveforms
  - EMG marking algorithm

Always look at waveforms!



  - Manual marking

CMAP, compound muscle action potential; EMG, electromyography.

Very Proximal Demyelination (Plexus/Roots)

- Stimulation at Erb's point and roots unreliable studies
  - Stimulator output insufficient at 100 mA/300 v @ 1.0 ms duration
- Imaging
  - Ultrasound: nerve cross-sectional enlargement
  - MRI: nerve enhancement

Caveats

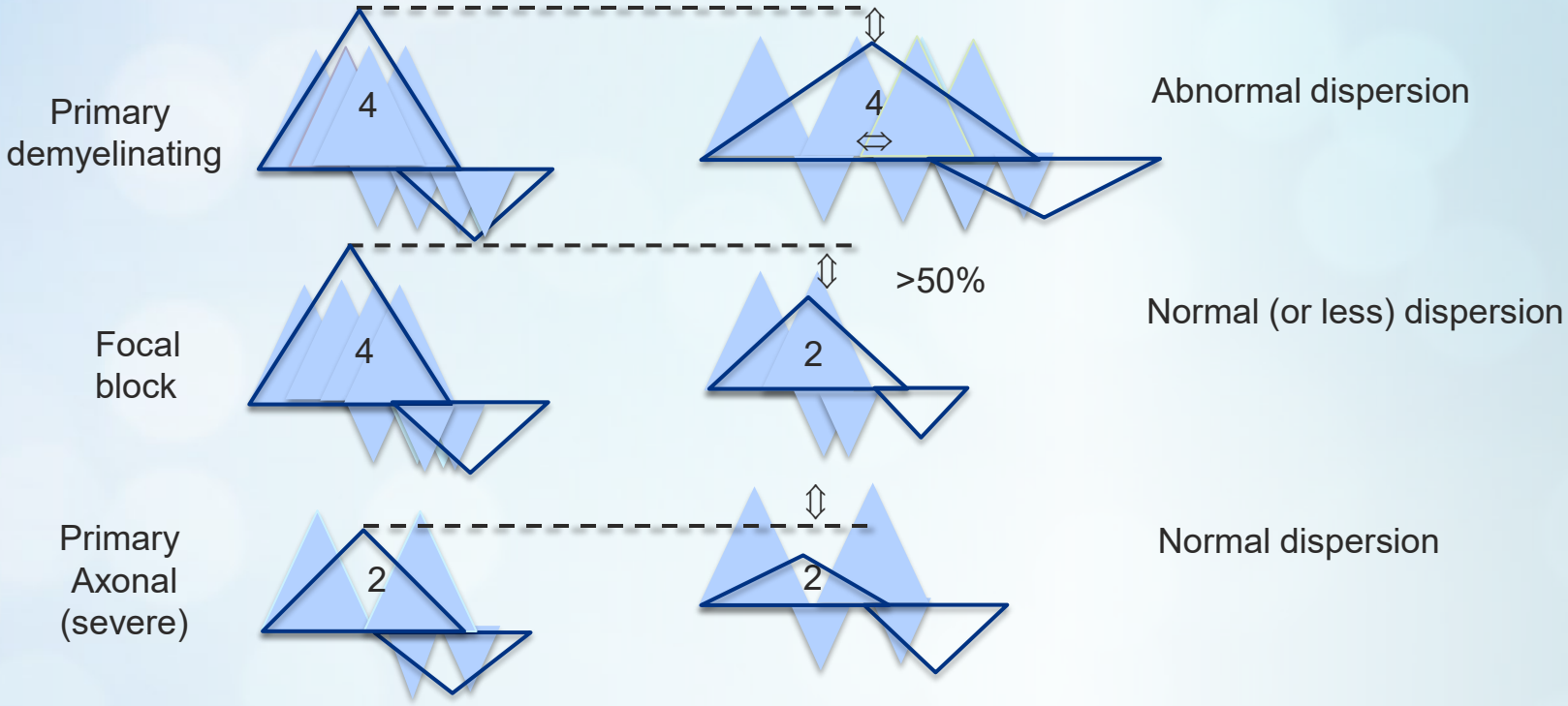
- Tibial nerve[1,2]
  - CMAP amplitude reduction to stimulation at knee in normal nerve due to E2 and volume conduction: ≠ conduction block
- Fibular nerve across fibular head
  - Possible site of entrapment
  - Difficult to stimulate in fossa and measure distance across knee for CV (adipose tissue obscures landmarks)
- Median nerve[2]
  - Overstimulation at wrist and axilla may activate neighboring ulnar nerve
- Axilla and Erb's point stimulation[2]
  - Difficult to stimulate median and ulnar nerves supramaximally

CMAP, compound muscle action potential; CV, conduction velocity.

References: 1. Barkhaus PE. *Muscle Nerve*. 2011;44(5):776-782.
2. Bromberg MB. *J Clin Neuromuscul Dis*. 2015;16(3):141-152.

Caveats: Conduction Block?

- Low (≤ 1mV) distal CMAP amplitude
  - Cannot assess for conduction block



Monitoring Follow-up: Nerve Conduction Studies?

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- Few well-conducted follow-up studies
  - Techniques not well described
    - ? Optimized CMAP amplitude (E1 electrode position)[1]
  - Techniques not fully reasonable
    - Distal CMAP comparisons with Erb's point CMAP
- Mixed results
  - ICE trial[2]
    - Variable changes in metrics (some improved/some worse)
    - Patients may be stable/better/worse
  - Improvements in other studies[3,4]
- Nerve conduction values not expected to resolve
  - In general, no utility to guide therapy

CMAP, compound muscle action potential; ICE, Immunoglobulin CIDP Efficacy.

References: 1. Bromberg MB. *Electroencephalogr Clin Neurophysiol.* 1997;105(5):385-389. **2.** Chin RL. *Muscle Nerve.* 2015;52(4):498-502. **3.** Bril V. *Muscle Nerve*. 2009;39(4):448-455. **4.** Cirillo G. *Muscle Nerve*. 2019;60(6):662-667.

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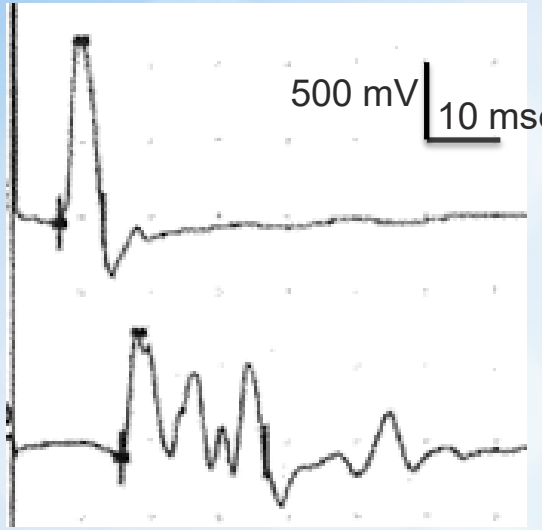
Summary

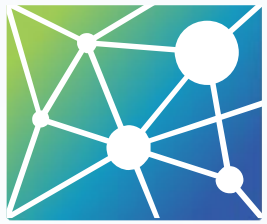
- Interpretation, interpretation, interpretation!
- *Clinical features*
- CMAP waveform
  - Amplitude – consider rise time, negative peak duration
- Assess for “greater slowing than expected for axonal loss”
  - Consider ALS-based guidelines ⇒ EAN/PNS criteria
- Attention to technical details

Postscript

- Do you agree with the conclusion: “Partial conduction block and increased temporal dispersion”



	Distal Lat (ms)	Duration (ms)	Amplitude (mV)	Area (mVms)	Conduction Vel (m/s)
Peroneal Ankle	6.5 (<5.7)	6.5	1.25 (>3.0)	4.21	
Peroneal Below Knee		20.9	0.85	7.1	33 (>40)



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