Challenges in Entrapments & Axonal vs. Demyelinating Neuropathies

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Phone: 1.416.597.9200
<table>
<thead>
<tr>
<th>PATTERN</th>
<th>Proximal</th>
<th>Distal</th>
<th>Asymm</th>
<th>Symm</th>
<th>Sensory Symptoms</th>
<th>Severe Proprioceptive Loss</th>
<th>UMN Signs</th>
<th>Autonomic Syms/Signs</th>
<th>DIAGNOSIS</th>
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<tbody>
<tr>
<td>NP1 - Symmetric prox &amp; distal weakness w/sensory loss</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>GBS/CIDP</td>
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<tr>
<td>NP2 - Distal sensory loss with/without weakness</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>CSPN, metabolic, drugs, hereditary, DADS</td>
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<tr>
<td>NP3 - Asymmetric distal weakness w/sensory loss</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
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<td>Multiple – vasculitis, HNPP, MADSAM, infection Single - Mononeuropathy, radiculopathy</td>
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<tr>
<td>NP4 - Asymmetric proximal &amp; distal weakness w/sensory loss</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
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<td>Polyradiculopathy, plexopathy</td>
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<tr>
<td>NP5 - Asymmetric distal weakness w/out sensory loss</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td>+/-</td>
<td>+ UMN – ALS/PLS - UMN – MMN</td>
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<tr>
<td>NP6 - Symmetric sensory loss &amp; upper motor neuron signs</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>B12/Copper deficiency; Friedreich's, Adrenomyeloneuropathy</td>
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<tr>
<td>NP7 - Symmetric weakness without sensory loss*</td>
<td>+-</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>Proximal &amp; Distal SMA Distal Hereditary motor neuropathy</td>
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<tr>
<td>NP8 - Focal midline proximal symmetric weakness*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+ UMN – ALS/PLS IBALS Kennedy’s Syndrome Bulbar GBS</td>
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<td>ALS ALS/PLS IBALS</td>
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<tr>
<td>NP9 - Asymmetric proprioceptive loss w/out weakness</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>Sensory neuronopathy (ganglionopathy) CISP</td>
</tr>
<tr>
<td>NP10 - Autonomic dysfunction</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>Diabetes, GBS, amyloid, prophyria</td>
</tr>
</tbody>
</table>

*Overlap patterns with myopathy and NMJ disorders

Adapted from Barohn RJ, Amato AA. Neurol Clin 2013;31(2):343-361.
<table>
<thead>
<tr>
<th>Pattern</th>
<th>Basic tests (in addition to EMG and Nerve Conduction Studies)</th>
<th>Optional Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP1</td>
<td>Serum immunofixation or SPEP, CSF</td>
<td>VEGF for POEMS, HIV</td>
</tr>
<tr>
<td>NP2</td>
<td>2 Hr OGTT or HgbA1c (possibly Fasting glucose), B12 with MMA, serum immunofixation or SPEP</td>
<td>RPR, SS-A/SS-B (SICCA), celiac panel and Vitamin E (diarrhea), ACE (resp), HIV (risk factor)</td>
</tr>
<tr>
<td>NP3</td>
<td>ESR, ANA, ANCA, RF, ds-DNA, ACE, SM, RNP, SS-A, SS-B, CCP Ab, Hep B/C, cryoglobulins, consider nerve and muscle biopsy</td>
<td>HIV, HNPP gene test, CSF for MADSAM</td>
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<tr>
<td>NP4</td>
<td>OGTT/ HgbA1c, CSF (if non-diabetic), lumbar spine and LS plexus imaging</td>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>NP5</td>
<td>Neuroimaging; If not hyperreflexic GM-1; If hyperreflexic copper, B12 and MMA</td>
<td>VLCFA, Friedreich's or SCA testing</td>
</tr>
<tr>
<td>NP6</td>
<td>B12, MMA, copper, C-spine or brain MRI</td>
<td></td>
</tr>
<tr>
<td>NP7</td>
<td>Acute/AMAN: CSF. Chronic: SMN gene, Kennedy's gene or HMN gene testing</td>
<td></td>
</tr>
<tr>
<td>NP8</td>
<td>Neuroimaging; If not hyperreflexic GM-1; If hyperreflexic copper, B12 and MMA</td>
<td></td>
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<tr>
<td>NP9</td>
<td>SS-A, SS-B, ACE, Anti Hu, Vitamin E, RPR</td>
<td>CSF, MRI with contrast of nerve roots and SSEPs for CISP</td>
</tr>
<tr>
<td>NP10</td>
<td>2 Hr OGTT or HgbA1c, B12 with MMA, serum immunofixation or SPEP, SS-A, SS-B, anti-Hu, Anti AchR nicotinic receptorAb</td>
<td>TTR, Alphagalactosidase, Porphyria, GAD-65, Autonomic testing</td>
</tr>
</tbody>
</table>
Case 1

- A 39 year old woman presents with 3 years h/o right medial proximal forearm pain exacerbated with activity

- Examination:
  - Normal strength, sensory and reflexes
  - Tenderness in the right medial forearm
  - Tinel sign over right medial forearm
  - Supination causes pain radiation to thumb

- What pattern?
  - NP3
Case 1

Which nerve is involved?

A. Median at the wrist / Carpal tunnel Sd
B. Median at the forearm
C. Median at the brachial plexus
D. Ulnar at the elbow
E. Radial at the spiral groove
Median Neuropathy at the Wrist aka Carpal Tunnel Syndrome

- The most common entrapment neuropathy
- Lifetime prevalence is 10%, 50% bilateral
- It is a clinical syndrome & mostly sensory
- Occasionally loss of dexterity due to weak opponens pollicis & APB
- Signs: Flick, Tinel & Phalen

Mendell, Kissel, Cornblath, Diagnosis & Management of Peripheral Nerve Disorders, 2001
Anterior Interosseous Syndrome

- Weak FPL, pronator quadratus & long flexor of index & middle fingers
- Pinch sign or OK sign, no sensory loss
- Pain is exacerbated by resisted proximal interphalangeal flexion of the middle finger
- DDX: ‘Forme fruste’ of neuralgic amyotrophy; MMN; mass lesion

Dimachkie MM. Median neuropathies other than carpal tunnel syndrome. In Medlink

- New data: median nerve fascicular involvement in the arm, predominantly at 14.6 ± 5.4 cm proximal to the humeroradial joint

Neurology. 2014 Feb 18;82(7):598-606
Median Neuropathies At The Forearm

- Trauma
- Compartment syndrome from blunt trauma
- Mass lesion: tumor, hematoma
- Electrical burn
- Multifocal motor neuropathy (MMN)
- Mononeuritis multiplex (50% of cases)
- Ischemic monomelic neuropathy / A-V fistula
- Thrombophlebitis of the median basilic vein
Sequence of NCS/EMG Changes In Acute Axon Loss Nerve Injury

- **Do not perform hyperacutely!**
- Day 0: Neurogenic firing
- Day 7: Reduced CMAP amplitude
- Day 11: Reduced SNAP amplitude in postganglionic lesion
- **Day 21: Fibrillation potentials**
- SNAP spared in preganglionic lesions
Basics of Nerve Conduction Studies
Chronic Focal Demyelination

- Slowing of nerve conduction velocity: **synchronized** or uniform loss of myelin from one axon to the next as in CMT

- Temporal dispersion: **non-uniform** or desynchronized loss of myelin from one axon to the next, leads to phase cancelation

- Conduction block: **focal & contiguous** demyelination of 2 or more internodes in ≥ 30-50% of axons
Response of PNS to Entrapments

- Slowed conduction velocity: most common finding in CTS and ulnar NP & correlates with numbness
- Slowed NCV is **NOT** a cause of weakness but either conduction block or axon loss **ARE**
- Axon loss is common in mononeuroapthies
- Reduction in SNAP and/or CMAP amplitude is proportional to degree of axon loss
CTS: Basic EDX Principles

- Sensory (mild) then motor latencies delays (moderate) →
- Sensory amplitudes decline (severe) →
- Motor amplitudes decline in more advanced cases
- Sensitivity of routine studies is only 60% for CTS
- Comparative motor and sensory studies increase sensitivity to 85%:
  - Transcarpal median & ulnar:
    - Motor: 2nd lumbrical to 2nd interosseus muscle
    - Sensory: Palmar orthodromic mixed
  - Transcarpal median & radial sensory responses
Neurogenic changes involving 2 muscles innervated by the **same** nerve root and **different** peripheral nerves
Case 1
Testing

- Routine nerve conduction studies: normal
- Needle EMG: normal
- GM1 antibody panel negative
Case 1

What would you do next?

A. Comparative and other nerve conductions
B. Carpal tunnel release
C. Reassurance & occupational therapy
D. MRI of forearm
E. Treat with intravenous immunoglobulin
Mass measuring 2.7 x 1.7 x 2.2 cm distal to the radial head and deep to the pronator teres. It is a fusiform mass continuous with the median nerve. There is on T1 signal central necrosis and moderate peripheral enhancement post contrast.
Forearm MRI

- Large fusiform, moderately enhancing mass in continuity with the median nerve
- The mass was successfully resected: benign nerve sheath schwannoma
- Post-operatively: all symptoms resolved
- What other diagnostic test could have been done?

Case 2

- A 56 yo man presents with left arm weakness
- Prior exposure to lead vapors but denied alcohol
- Examination:
  - Finger abduction 3/5 (cannot lift wrist)
  - Wrist and finger extensors 2/5
  - Distal interphalangeal extension 2/5
    - With wrist & metacarpophalangeal joints passively extended, distal interphalangeal extension becomes normal
  - Pinprick reduced over dorsal first web space
  - Normal reflexes
  - NP3
Case 2

Which nerve is involved?

A. Median at the wrist / Carpal tunnel Sd
B. Ulnar at the elbow
C. Ulnar at the wrist
D. Ulnar at the brachial plexus
E. Radial at the spiral groove
Ulnar Neuropathy at the Elbow

- The 2\textsuperscript{nd} most common arm entrapment NP
- Often bilateral

- Multiple Sites:
  - Proximal ulnar groove at the elbow is the most common entrapment site
  - Cubital tunnel
  - Compression in the wrist and hand

- Etiologies: external compression, repetitive traction (elbow), internal compression (ganglia, tumors, fibrous bands)

Stewart, Focal Peripheral Neuropathies, 2010
Ulnar Neuropathy at the Elbow

Presentation

- Numbness in the little finger
- Lack of dexterity / reduced grip
- Weak finger abd/adduction & digits 4, 5 flexion
- Elbow pain
- Claw hand
- Froment’s sign

Dimachkie MM. Ulnar Neuropathy at the elbow. In Medlink. Arbor publishing Corp., 2014

Stewart, Focal Peripheral Neuropathies, 2010
Ulnar Neuropathy at the Elbow

Predisposing Conditions
- Chronic compression
- Diabetes mellitus
- HNPP
- Elbow condylar or humeral fracture
- Elbow deformity: RA, OA, valgus, Paget’s
- Leprosy
- Ulnar nerve prolapse
- Supracondylar spur
- Mass lesion

“Purely Motor”
- Motor neuron disease
- MMN is less common
- C8 radiculopathy rarely
- Syrinx
- Stroke
- Neurogenic TOS / lower trunk brachial plexopathy

Dimachkie MM. Ulnar Neuropathy at the elbow. In Medlink. Arbor publishing Corp., 2015
Ulnar Neuropathy at the Elbow
NCS

- Slowing of ulnar NCV across the elbow
ABSTRACT: Patients with clinical evidence of ulnar mononeuropathy at the elbow may have normal routine motor and sensory nerve conduction studies, suggesting a low sensitivity for these methods. Other, more specialized techniques may have a higher sensitivity, increasing diagnostic yield, and provide more specific localization of the lesion. We compared the sensitivity and specificity of ulnar segmental nerve conduction studies (SgNCS or "inching") at 2-cm intervals with those of routine ulnar motor and sensory studies. We studied 21 arms with symptoms or signs of ulnar neuropathy and 25 asymptomatic control arms. SgNCS proved significantly more sensitive than more routine studies in diagnosing ulnar neuropathy at the elbow, with a sensitivity of 81%, whereas motor conduction velocity in a longer (10–14 cm) segment across the elbow was the next most sensitive at 24%. Recording from the first dorsal interosseous muscle did not improve sensitivity when compared with recording from the abductor digiti quinti. Short SgNCS significantly improves detection of ulnar mononeuropathy at the elbow and should be considered when routine studies are negative and clinical suspicion remains high.


THE UTILITY OF SEGMENTAL NERVE CONDUCTION STUDIES IN ULNAR MONONEUROPATHY AT THE ELBOW

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and CLIFTON GOOCH, MD2

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Accepted 11 September 2002

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<td>D6</td>
<td>8.3 ms</td>
<td>1.2 mV</td>
<td>-2.6</td>
<td>mm</td>
<td>m/s</td>
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<tr>
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<td>1.1 mV</td>
<td>-2.5</td>
<td>mm</td>
<td>m/s</td>
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<td>D2</td>
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<td>1.2 mV</td>
<td>-2.5</td>
<td>mm</td>
<td>m/s</td>
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<td>P</td>
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<td>mm</td>
<td>m/s</td>
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<td>P2</td>
<td>16.4 ms</td>
<td>0.6 mV</td>
<td>-2.8</td>
<td>mm</td>
<td>m/s</td>
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<td>16.6 ms</td>
<td>0.6 mV</td>
<td>-2.7</td>
<td>mm</td>
<td>m/s</td>
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<tr>
<td>P6</td>
<td>17.4 ms</td>
<td>0.6 mV</td>
<td>-2.7</td>
<td>mm</td>
<td>m/s</td>
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</table>
Case 2

Routine NCS is normal. What would you do next?

A. Inching of ulnar nerve at the elbow
B. Test the radial n. at the spiral groove
C. MRI of forearm
D. Reassurance & occupational therapy
E. Treat with intravenous immunoglobulin
Radial Neuropathy
Mechanisms

- Compression: sleep / tourniquet / muscular
- 15% of all humeral fracture accounting for 25% of radial NP
- Systemic disease: diabetes, MMN, leprosy
- Lead poisoning spares brachioradialis (BR) muscle
- Blunt or birth trauma
- Tumor, cyst or lipoma
- Entrapment at Arcade of Frohse
Saturday Night Palsy

- 50% of all radial neuropathies
- Sunderland 1945
- Radial nerve compression at spiral groove
- Back of the chair or bed partner
- Painless wrist and finger drop
- Paresthesias of wrist dorsum
- Good prognosis

Saturday Night Palsy Examination

- Triceps and anconeus sparing
- Flaccid BR during elbow flexion (82%)
- Weak wrist and finger extension
- Reduced pin over dorsum of metacarpal joints 1 & 2 (60%)
- “Weak” interossei
- Spared distal phalangeal extension
Posterior Interosseous Neuropathy

- Deep motor branch, no sensory involvement
- Wrist/finger drop with radial wrist deviation on wrist extension due to ECR sparing
- Previously thought to be due to compression at fibrous edge of the arcade of Frohse or more distally in supinator
- New data: lesion is in most cases (84%) located 8.3 cm proximal to elbow joint vs. 14% at supinator channel

*Neurology 2016;87:1884–1891*
Case 2
Tests

- More history: awoke with it 3 weeks ago
- GM1 negative
- Routine left arm nerve conduction studies were normal
- NEE fib. in left:
  - BR
  - EDC
  - Sparing triceps
Case 2

- Mechanical disadvantage limits hand strength testing in radial neuropathy pseudo-weakness in:
  - finger abduction &
  - distal phalangeal extension

- Wrist extension on a flat surface normalizes interosseous muscle strength (ulnar n.)

- Wrist & metacarpophalangeal joints extension normalizes distal interphalangeal joint extension which is innervated by what nerve(s)?
Case 3

- 54 yo woman with acute left foot drop x 1 month and chronic low back pain x 2 years
- PMH: left breast cancer s/p mastectomy and hormonal therapy, recent weight loss
- Exam:
  - Ankle dorsiflexion & toe extension 2/5
  - Foot inversion 4/5
  - Decreased pin perception on left foot dorsum
  - NP3
Case 3

Which test would you order?

A. EMG
B. Nerve conduction studies
C. MRI lumbar spine
D. MRI lumbosacral plexus
E. GM1 antibody panel
Clinical Presentation
Common Peroneal Neuropathy

- Most common peripheral nerve entrapment of the leg
- Acute or subacute foot drop
- Non progressive
- Foot numbness
- Painless except with mass lesion
- 10% bilateral

Mendell, Kissel, Cornblath  Diagnosis & Management of Peripheral Nerve Disorders, 2001
Case 3
NCS

MNC Record #1
Peroneal nerve L
14:29:19

Switch: N-R
Stim: 1
Rate: Non-Recruent
Level: 177 V
Dur: 0.3 ms
Single
Step: 1
Average: Off
Rectify: Off

Recording Site: EDB

Stimulus Site
<table>
<thead>
<tr>
<th>Lat ms</th>
<th>Dur ms</th>
<th>Amp mV</th>
<th>Area mV ms</th>
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</thead>
<tbody>
<tr>
<td>A1: Ankle</td>
<td>4.8</td>
<td>7.0</td>
<td>2.4</td>
</tr>
<tr>
<td>A2: Fibular head</td>
<td>11.2</td>
<td>8.8</td>
<td>2.3</td>
</tr>
<tr>
<td>A3: Knee</td>
<td>13.2</td>
<td>8.5</td>
<td>0.8</td>
</tr>
<tr>
<td>A4: Ankle</td>
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Segment
<table>
<thead>
<tr>
<th>Dist mm</th>
<th>CV m/s</th>
<th>CV m/s</th>
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</thead>
<tbody>
<tr>
<td>Ankle-Fibular head</td>
<td>280</td>
<td>6.4</td>
</tr>
<tr>
<td>Fibular head-Knee</td>
<td>100</td>
<td>2.0</td>
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</tbody>
</table>

MNC Record #5
Peroneal nerve L
15:40:32

Switch: N-R
Stim: 1
Rate: Non-Recruent
Level: 320 V
Dur: 0.1 ms
Single
Step: 3
Average: Off
Rectify: Off

Recording Site: T.A.

Stimulus Site
<table>
<thead>
<tr>
<th>Lat ms</th>
<th>Dur ms</th>
<th>Amp mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1: Knee</td>
<td>4.3</td>
<td>19.6</td>
</tr>
<tr>
<td>A2: Above Knee</td>
<td>8.3</td>
<td>19.0</td>
</tr>
<tr>
<td>A3:</td>
<td></td>
<td></td>
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Segment
<table>
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<tr>
<th>Dist mm</th>
<th>CV m/s</th>
<th>Target CV m/s</th>
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<tbody>
<tr>
<td>Knee-Above Knee</td>
<td>120</td>
<td>30</td>
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</table>
Common Peroneal Neuropathy
Associated Conditions

- Weight loss
- Compression
  - Leg crossing, squatting, braces, bandage, cast
  - Surgical procedures / anesthesia
  - Coma
- Diabetes mellitus, HNPP
- Trauma / fracture
- Ganglion cyst & nerve tumor slowly progressive
- Weight loss & leg crossing triggered this case
Case 3  
Pearls & Oysters

• Always passively dorsiflex the ankle when testing ankle inversion in pts with foot drop

• In peroneal NP, ankle dorsiflexion weakness is of same degree as toe extension

• In L5 radiculopathy, big toe extension is weaker than ankle dorsiflexion since EHL has more L5 root innervation

• If painful (exclude MM), progressive or no clear trigger, look for mass lesion via ultrasound
How To Interpret NCS for Demyelination

- Depends on clinical presentation
- Depends on degree of axonal loss
- Consider criteria for demyelination
- Decide if this is a treatable neuropathy and a trial of immune therapy is indicated
### Axon Loss or Demyelination?
Interpreting NCS When Amplitudes are Small

<table>
<thead>
<tr>
<th>%</th>
<th>NCV (m/sec)</th>
<th>DL (msec)</th>
<th>F WAVE (msec)</th>
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<tbody>
<tr>
<td></td>
<td>LLN</td>
<td>&lt;80&lt;sup&gt;1&lt;/sup&gt;</td>
<td>&lt;70&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>Med</td>
<td>49</td>
<td>39.2</td>
<td>34.3</td>
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<tr>
<td>Uln</td>
<td>50</td>
<td>40.0</td>
<td>35.0</td>
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<tr>
<td>Per</td>
<td>41</td>
<td>32.8</td>
<td>28.7</td>
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<tr>
<td>Tib</td>
<td>41</td>
<td>32.8</td>
<td>28.7</td>
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</table>

<sup>1</sup> = If Amp > 80% LLN  
<sup>2</sup> = If Amp < 80% LLN

**If:**
- Median CMAP LLN 4.5 mV; then 80% LLN = 3.6 mV
- Ulnar CMAP LLN 5.0 mV; then 80% LLN = 4 mV
- Peroneal CMAP LLN 2.0 mV; then 80% LLN = 1.6 mV
- Tibial CMAP LLN 4.0 mV; then 80% LLN = 3.2 mV

Demyelination: You know it when you see it!
Commonly Mentioned Criteria

- AAN criteria; 6 to 7 findings:
  - Low sensitivity about 40%
  
- INCAT; 3 different nerves

- EFNS/PNS; Only 2 different nerves BUT:
  - More strict degree of nerve conduction slowing
  - Introduces duration of distal CMAP response:
    increase in ≥1 nerve (median ≥6.6 ms, ulnar ≥6.7 ms, peroneal ≥7.6 ms, tibial ≥8.8 ms) + ≥1 other demyelinating parameter in ≥1 other nerve

References:
- Neurology 1991 May;41(5):617-8
- Hughes et al Ann N 2001 50 (2)195-201
Sensitivity vs Specificity

- Sensitive criteria
  - Less strict cutoffs
  - i.e. Define CB as a 30% drop rather than 50%
  - Require fewer abnormalities/nerves affected
  - But, less specific and will diagnose diabetic NP, CSPN or ALS as “demyelinating”

- More stringent criteria
  - More abnormalities needed and more specific
  - Might miss real cases

- Use your common sense
Technical Factors in Testing

- Cold skin temperature (hand < 32°C or leg < 30°C):
  - Slows NCV due to slowed Na channel function
  - Prolonged distal latencies & slowed NCV

- Distance measurements over shorter segments

- Pseudo-conduction block:
  - Martin-Gruber anastomosis
  - Overstimulation at distal sites
The Clinical Exam

- In “classic CIDP” (NP1) with proximal and distal weakness should have high index of suspicion even if the NCS do not show much demyelination

- In a diabetic neuropathy or CSPN (NP2), even moderate evidence of demyelination probably does not mean CADP:
  - These are much more common than sensory CIDP or DADS

- EDX Criteria alone cannot make a “diagnosis”

- Clinical findings:
  - predict the likelihood of treatment response and
  - guide changes in treatment