Distally Predominant, Symmetrical, Axonal Polyneuropathies – an overview

Introduction –

The words "Neuropathy," "Polyneuropathy" and "Peripheral Neuropathy" actually encompass many different disorders. They may include systemic, infectious or inflammatory causes. These several categories could include hereditary motor and sensory neuropathies or acquired neuropathies secondary to toxic exposure or even as a side effect of some drugs.

This paper focuses on the distally predominant, symmetrical and primarily axonal neuropathies (DSPN) that are common in the NCS/EMG laboratory and are associated with systemic or metabolic diseases such as diabetes. This is not to discount all the other findings and symptoms of polyneuropathies. Other causes of neuropathy as well as hereditary causes will be addressed in subsequent papers.

Diabetic polyneuropathy is the most common polyneuropathy in the United States. Other causes of systemic and metabolic causes of polyneuropathy might include renal failure, uremia, hepatic disorders and critical care illnesses.

This paper will look at the clinical presentation, differential diagnosis, specifics of NCS/EMG testing and case studies.

Clinical Presentation –

Diabetes is not a new condition and the relative association to nervous system changes has been evident for more than a century and a half. Loss of deep tendon reflexes and impaired vibration in the lower extremities in patients with a long history of diabetes is well documented. Studies show that half to two-thirds of all diabetic patients will suffer from neuropathy. Varying degrees of both small and large fiber involvement is seen.

Occasionally a very mild or asymptomatic polyneuropathy is discovered in the EMG lab when investigating another group of symptoms, such as carpal tunnel syndrome. More often, however, patients present with a variety of symptoms that suggest peripheral nerve disease, such as distal paresthesias.

The symptoms may take years to develop. Distal paresthesias and distal weakness are the most common complaints. Loss of vibratory and position sense can be present, but is less common. It is believed that the distal predominance is related to the axon length; the longer the axon the greater it is affected. It is generally accepted when the paresthesias reach approximately mid-calf, sensory symptoms become evident in the hands. This is referred to as the "stocking-glove" distribution. Motor involvement with frank weakness can occur in the same pattern, but only later and in more severe cases.

On examination, distal loss of sensation to pin prick, light touch, vibration, cold and proprioception occur in the "stocking-glove" distribution and tends to be similar to the subjective complaints. Decreased or absent ankle reflexes occur early in the disease, while more widespread loss of reflexes and motor weakness are late findings. Motor examination may disclose wasting of the intrinsic muscles of the feet or lower leg; similar findings are evident in the hands in more severe cases.

Differential Diagnosis –

The key in separating distally predominant, symmetrical axonal neuropathies from other conditions are time course, the sensory more than motor symptoms and the symmetry of the symptoms.

Guillain-Barré has an acute and rapid onset, while CIDP has a gradual onset. The inclusion of motor symptoms helps it stand out versus DSPN's. Mononeuropathy multiplex can closely resemble DSPN but is not symmetrical. Mononeuropathy multiplex presents with multiple mononeuropathies with involvement of entirely unrelated nerves, such as the median nerve in the arm and the tibial nerve in the leg. If more proximal signs are present alarm bells should ring for an alternate or secondary cause.

Specific Nerve Conduction Studies –

The most common way to sort out these different types of polyneuropathies is the NCS/EMG. There are specific and fairly standard test protocols for DSPN.

It is generally accepted that NCS examination of 3 extremities is required to prove distal predominance and symmetry. Unless there is a compelling reason to choose otherwise (i.e. leg amputation) these limbs would include both legs and one arm. If an asymmetry exists, additional or alternate explanations could necessitate additional testing.

In the legs:

The sural sensory nerve is important as it is a long and a purely sensory nerve. In a patient with a DSPN one would expect reduced amplitude with a normal or very near normal latency and/or conduction velocity. As the disease progresses the sural sensory nerve may be non-recordable. In general, these findings hold true for additional sensory nerves you may examine. The superficial peroneal and medial plantar nerves may be useful especially when looking for mild DSPN. Averaging of the lower extremity sensory responses is often necessary and many labs average routinely.

The peroneal motor nerve (sometimes called fibular nerve) should be recorded over the extensor digitorum brevis (EDB). The three standard stimulation sites, ankle, fibular head and above knee sites should be recorded. The findings may stay in the normal range in the earliest stages of DSPN. Reduced amplitude with normal or near normal latencies and conduction velocities are the usual findings in modest DSPN, while additional amplitude reduction and CV slowing in all segments is seen as the disease progresses. If the response to the EDB is absent or very low amplitude the peroneal nerve recording from

the tibialis anterior (TA) is useful as it is more proximal. It is logical that the CMAP amplitude would be greater when recording over the TA. If, on this examination, focal conduction velocity slowing or a focal conduction block is seen, consider an alternative or an additional problem (i.e. peroneal neuropathy at the fibular head).

Peroneal F-wave is considered helpful in separating proximal from distal conditions and is usually mildly prolonged is DSPN's. The peroneal F-wave, however, can be fickle and is not always recordable, especially if there is reduced distal amplitude.

The tibial motor nerve is recorded over the abductor hallucis (AH) and stimulated at the ankle, behind the medial malleolus, and in the popliteal fossa. The findings may stay in the normal range in the earliest stages of DSPN. Reduced amplitude with normal or near normal latencies and conduction velocities are common as the disease progresses. The tibial CMAP seems to remain normal or near normal well into the disease process.

Tibial F-wave is considered helpful in separating proximal from distal conditions and is usually mildly prolonged is DSPN's.

To evaluate and prove symmetry at least one sensory and one motor nerve should be done on the opposite leg. If asymmetries (i.e. amplitude differences of more than 50%) are observed, additional testing would be indicated.

In the arms:
The median sensory nerve should be studied in your usual fashion, either antidromically or orthodromically. The longer segment from the wrist to digit II or III (12-14 cm) is preferable to the palmar studies. In a patient with a DSPN one would expect reduced amplitude with a normal or very near normal latency and/or conduction velocity. It is expected this reduced amplitude, however, would be less dramatic than the amplitude reduction of the sural or superficial peroneal nerves in the legs.

The ulnar sensory nerve should be studied in your usual fashion, either antidromically or orthodromically. The longer segment from the wrist to digit V (11-13 cm) is preferable to the palmar studies. In a patient with a DSPN one would expect reduced amplitude with a normal or very near normal latency and/or conduction velocity. It is expected this reduced amplitude, however, would be less dramatic than the amplitude reduction of the sural or superficial peroneal nerves in the legs.

The radial sensory nerve should be studied in your usual fashion and is useful because both the median and ulnar nerves are prone to entrapment neuropathies and the radial less so. In a patient with DSPN, reduced amplitude may be present and this reduction becomes more obvious as the disease progresses. Latency and/or conduction velocity is generally preserved.

There is a well documented increased incidence of carpal tunnel syndrome in patients with distally predominant, symmetrical axonal neuropathies. Thus if there is a prolonged

distal latency of the median nerve a further examination such as the transcarpal, median to ulnar comparison may be indicated.

The median motor nerve should be studied recording over the abductor pollicis brevis (APB). Stimulation at the wrist and elbow should be recorded. The findings remain normal in early DSPN and usually only show amplitude reduction in the most advanced cases. If a prolonged latency is present consider the possibility of an underlying condition, such as carpal tunnel syndrome.

Median F-wave is considered helpful in separating proximal from distal conditions and is usually mildly prolonged is DSPN's. Care should be taken when a CTS is present as the prolonged F-wave may simply indicate the slowing in the distal segment.

The ulnar motor nerve should be studied recording over the abductor digiti minimi (ADM). Stimulation at the wrist, below and above the elbow should be recorded. The findings remain normal in early DSPN and usually only show amplitude reduction in the most advanced cases. If slowed conduction velocity or focal amplitude reduction is present consider the possibility of an underlying conduction, such as ulnar neuropathy at the elbow.

Ulnar F-wave is considered helpful in separating proximal from distal conditions and is usually mildly prolonged is DSPN's. Care should be taken when an ulnar neuropathy is present as the prolonged F-wave may simply indicate the slowing in the across elbow segment.

Case Studies –

Case 1

Mild distally predominant, symmetrical and primarily axonal neuropathy

		Temperatures:
Date of Birth:	8/6/1948	Left wrist: 32°C
Age:	60	Right leg: 32.5°C
Gender:	Male	Left leg: 33.5°C

REASON FOR STUDY: History of right hand weakness and fasciculations in the proximal arms for many years. Patient was recently diagnosed with Parkinsonism and responded somewhat to Sinemet. Reflexes are reduced in the left arm and can be elicited at both ankles. There is no pathological spread. The current study is requested to evaluate for underlying neuropathic changes.

CLINICAL CORRELATION:

There is electrical evidence to suggest the presence of a mild, generalized, length-dependent, relatively symmetric, predominately sensory axonal polyneuropathy. The differential diagnosis of this pattern is extensive and includes nutritional deficiencies, alcoholism, connective tissue disorders, toxic, metabolic and drug induced neuropathies, HIV, lymphomatous and carcinomatous neuropathies, and selected other rare conditions.

Abnormal values are in **Bold**

Motor Nerve Conduction:

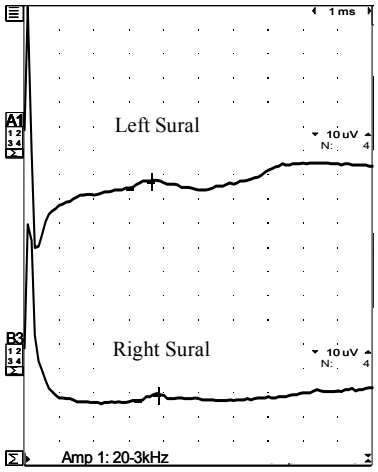
Nerve and Site	Segment	Distance	Latency	Amplitude	Conduction Velocity
Right Peroneal					
Ankle	Extensor digitorum brevis-Ankle	90 mm	5.4 ms	2.02 mV	
Fibula (head)	Ankle-Fibula (head)	320 mm	12.5 ms	1.96 mV	45.0 m/s
Popliteal fossa	Fibula (head)-Popliteal fossa	100 mm	14.5 ms	1.93 mV	50.0 m/s
Right Tibial					
Ankle	Abductor hallucis-Ankle	100 mm	5.0 ms	7.97 mV	
Popliteal fossa	Ankle-Popliteal fossa	445 mm	14.7 ms	4.96 mV	45.8 m/s
Left Peroneal					
Ankle	Extensor digitorum brevis-Ankle	90 mm	4.3 ms	4.91 mV	
Fibula (head)	Ankle-Fibula (head)	330 mm	11.9 ms	4.18 mV	43.4 m/s
Popliteal fossa	Fibula (head)-Popliteal fossa	100 mm	13.9 ms	3.96 mV	50.0 m/s
Left Tibial					
Ankle	Abductor hallucis-Ankle	100 mm	4.4 ms	6.85 mV	
Popliteal fossa	Ankle-Popliteal fossa	430 mm	14.3 ms	4.13 mV	43.4 m/s
Left Median					
Wrist	Abductor pollicis brevis-Wrist	60 mm	3.4 ms	13.32 mV	
Elbow	Wrist-Elbow	265 mm	8.6 ms	13.18 mV	50.9 m/s
Axilla	Elbow-Axilla	170 mm	11.6 ms	12.71 mV	56.6 m/s
Left Ulnar					
Wrist	ADM-Wrist	60 mm	2.7 ms	11.65 mV	
Below elbow	Wrist-Below elbow	265 mm	7.8 ms	10.61 mV	51.5 m/s
Above elbow	Below elbow-Above elbow	100 mm	9.7 ms	9.86 mV	53.7 m/s
Axilla	Above elbow-Axilla	135 mm	11.9 ms	9.58 mV	61.3 m/s

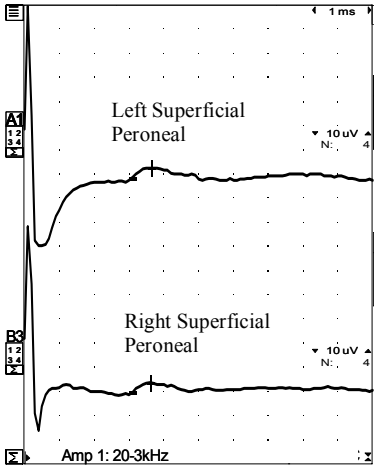
F-Wave Studies

Nerve	M-Latency	F-Latency
Right Peroneal	5.4 ms	**57.3 ms**
Right Tibial	5.0 ms	53.0 ms
Left Peroneal	4.3 ms	52.3 ms
Left Tibial	4.4 ms	55.1 ms
Left Median	3.4 ms	30.5 ms
Left Ulnar	11.9 ms	30.6 ms

Sensory Nerve Conduction:

Nerve and Site	Segment	Distance	Amplitude	Peak Latency
Left Radial				
Forearm	Anatomical snuff box-Forearm	100 mm	19.8 µV	2.4 ms
Left Sural				
Lower leg	Lateral malleolus-Lower leg	140 mm	**3.0 µV**	3.6 ms
Right Sural				
Lower leg	Lateral malleolus-Lower leg	140 mm	**2.6 µV**	3.8 ms
Left Superficial Peroneal				
Lower leg	Ankle-Lower leg	140 mm	**4.1 µV**	3.6 ms
Right Superficial Peroneal				
Lower leg	Ankle-Lower leg	140 mm	**4.1 µV**	3.6 ms
Left Median				
Digit II (index finger)	Wrist-Digit II (index finger)	130 mm	**11.2 µV**	2.9 ms
Left Ulnar				
Digit V (little finger)	Wrist-Digit V (little finger)	110 mm	**4.2 µV**	3.1 ms


Left Sural
Right Sural
Amp 1: 20-3kHz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Right Superficial Peroneal
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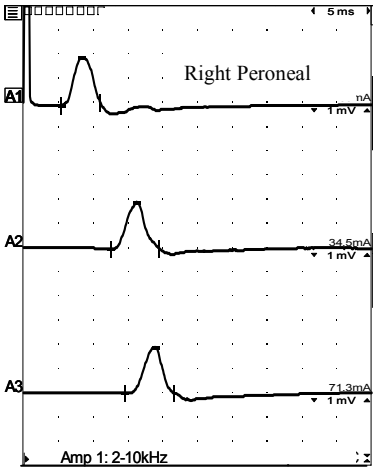
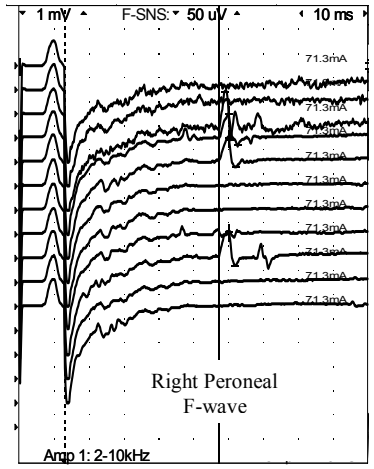
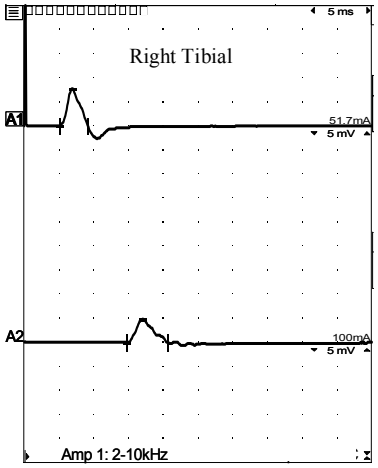
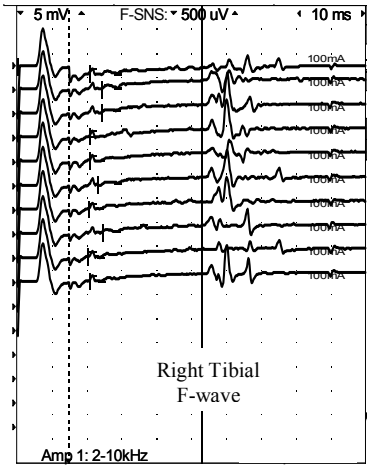

Right Peroneal
Amp 1: 2-10kHz


Right Peroneal F-wave
Amp 1: 2-10kHz


Right Tibial
Amp 1: 2-10kHz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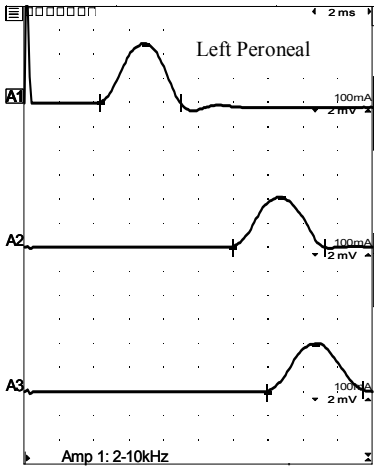
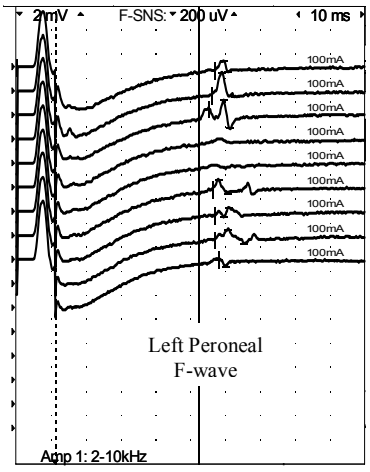
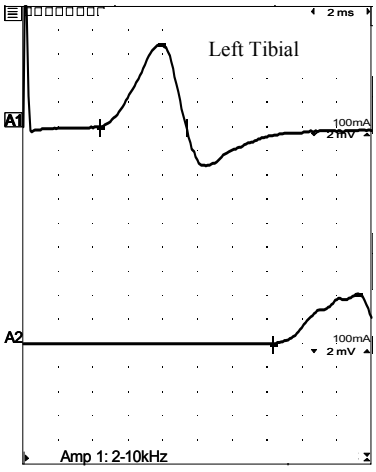
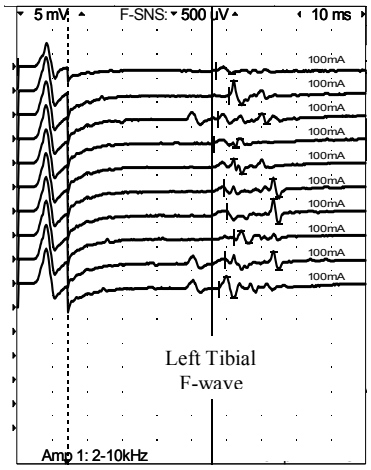
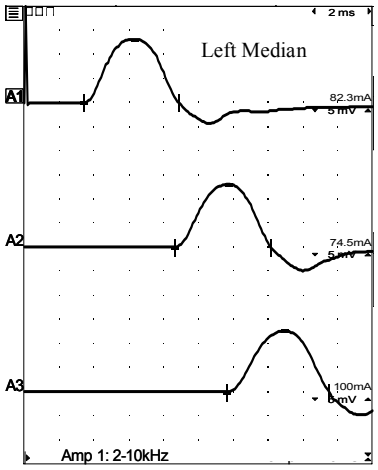
Amp 1: 2-10kHz

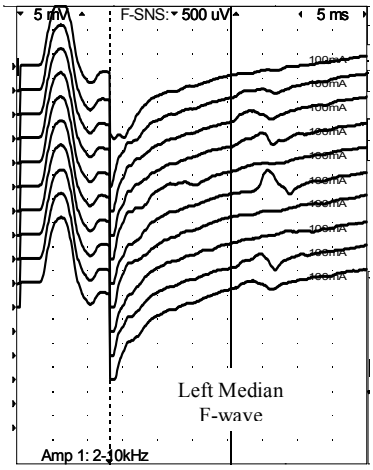

Left Peroneal
Amp 1: 2-10kHz

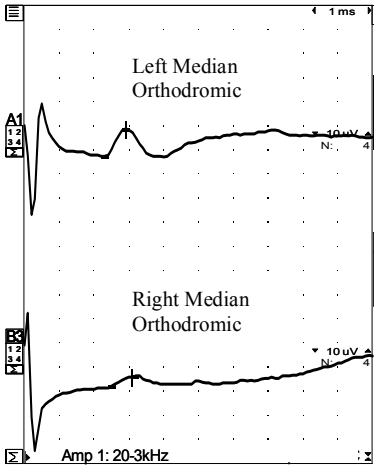

Left Peroneal F-wave
Amp 1: 2-10kHz

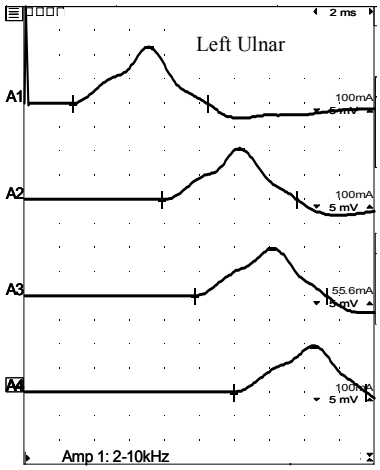

Left Tibial
Amp 1: 2-10kHz

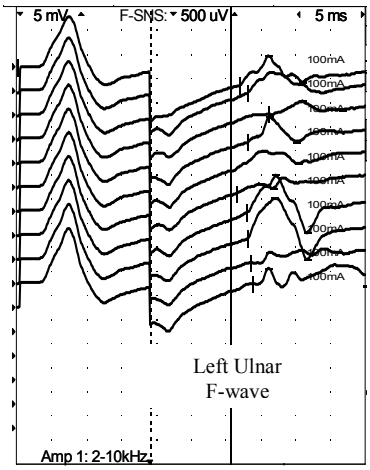












Case 2

Moderate to severe distally predominant, symmetrical and primarily axonal neuropathy

		Temperatures:
Date of Birth:	5/24/1940	Right wrist: 31.5°C
Age:	69	Right leg: 31°C
Gender:	Male	Left leg: 31.5°C

REASON FOR STUDY: History of long-standing leg cramps and 5 year history of leg weakness. Evaluate for underlying neuropathic or myopathic process.

CLINICAL CORRELATION:

This is an abnormal study. There is electrical evidence to suggest the presence of the presence of a generalized, chronic, length-dependent, relatively symmetric, mixed sensory and motor axonal polyneuropathy. The differential diagnosis of this pattern is extensive and includes nutritional deficiencies, alcoholism, connective tissue disorders, toxic, metabolic and drug induced neuropathies, HIV, lymphomatous and carcinomatous neuropathies, and selected other rare conditions.

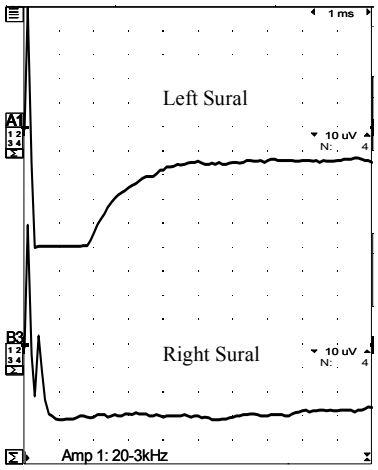
Abnormal values are in **Bold**

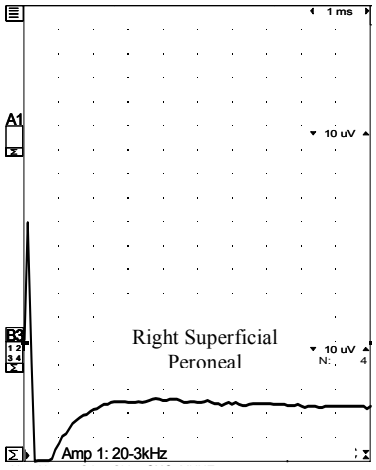
Motor Nerve Conduction:

Nerve and Site	Segment	Distance	Latency	Amplitude	Conduction Velocity
Right Peroneal					
Ankle	Extensor digitorum brevis-Ankle	90 mm	**7.4 ms**	**0.07 mV**	
Right Peroneal					
Fibula (head)	Tibialis anterior-Popliteal fossa		3.6 ms	**1.37 mV**	
Popliteal fossa	Fibula (head)-Popliteal fossa	100 mm	5.5 ms	**1.35 mV**	52.6 m/s
Right Tibial					
Ankle	Abductor hallucis-Ankle	100 mm	5.6 ms	**0.41 mV**	
Popliteal fossa	Ankle-Popliteal fossa	420 mm	14.2 ms	**0.28 mV**	48.8 m/s
Right Median					
Wrist	Abductor pollicis brevis-Wrist	60 mm	4.2 ms	6.08 mV	
Elbow	Wrist-Elbow	270 mm	9.7 ms	5.63 mV	49.0 m/s
Right Ulnar					
Wrist	ADM-Wrist	60 mm	3.2 ms	**5.48 mV**	
Below elbow	Wrist-Below elbow	240 mm	8.0 ms	**5.50 mV**	50.0 m/s
Above elbow	Below elbow-Above elbow	100 mm	9.9 ms	**5.39 mV**	52.6 m/s
Left Peroneal					
Ankle	Extensor digitorum brevis-Ankle	90 mm	6.6 ms	**0.09 mV**	
Left Peroneal					
Fibula (head)	Tibialis anterior-Popliteal fossa		3.8 ms	**0.96 mV**	
Popliteal fossa	Fibula (head)-Popliteal fossa	100 mm	5.6 ms	**0.88 mV**	55.5 m/s
Left Tibial					
Ankle	Abductor hallucis-Ankle	100 mm	5.6 ms	**0.32 mV**	

Sensory Nerve Conduction:

Nerve and Site	Segment	Distance	Amplitude	Peak Latency
Left Sural				
Lower leg	Lateral malleolus-Lower leg	140 mm	**NR**	**NR**
Right Sural				
Lower leg	Lateral malleolus-Lower leg	140 mm	**NR**	**NR**
Right Superficial Peroneal				
Lower leg	Ankle-Lower leg	140 mm	**NR**	**NR**
Right Median				
Digit II (index fing	Wrist-Digit II (index finger)	130 mm	**5.5 µV**	**3.7 ms**
Right Ulnar				
Digit V (little fing	Wrist-Digit V (little finger)	110 mm	**4.0 µV**	2.8 ms
Right Transcarpal, Med-Uln Comparison				
Mid palm (Median)	Wrist-Mid palm (Median)	80 mm	15.0 µV	**2.5 ms**
Mid palm (Ulnar)	Wrist-Mid palm (Ulnar)	80 mm	5.6 µV	2.0 ms
Right Radial				
Forearm	Anatomical snuff box-Forearm	100 mm	**12.1 µV**	2.7 ms


Left Sural
Right Sural
Amp 1: 20-3kHz


Right Superficial Peroneal
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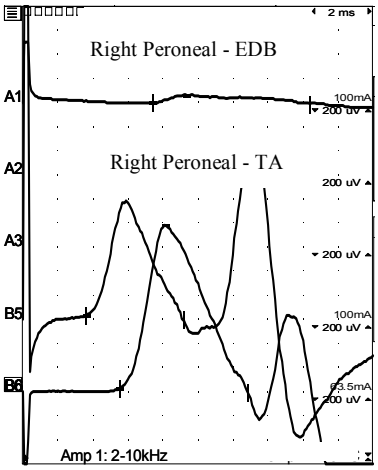
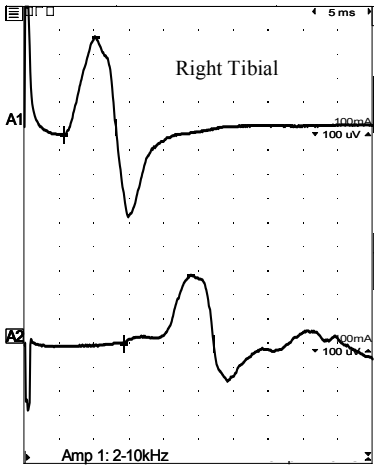
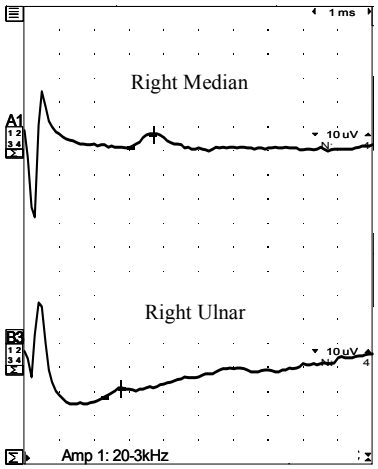
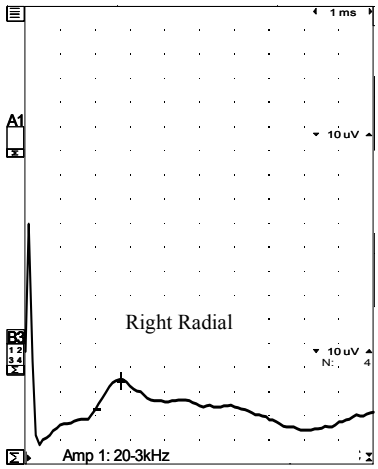
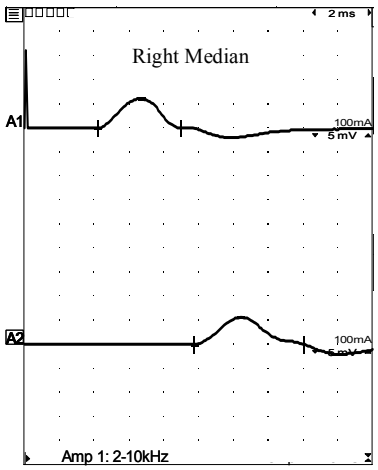
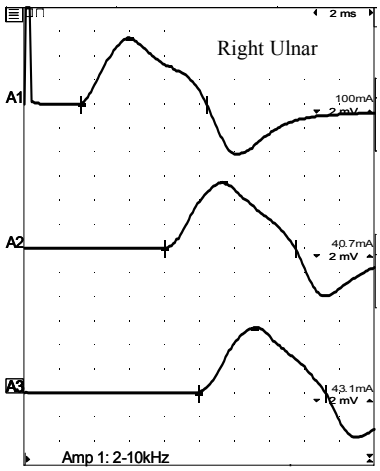

Right Peroneal - EDB
Right Peroneal - TA
Amp 1: 2-10kHz

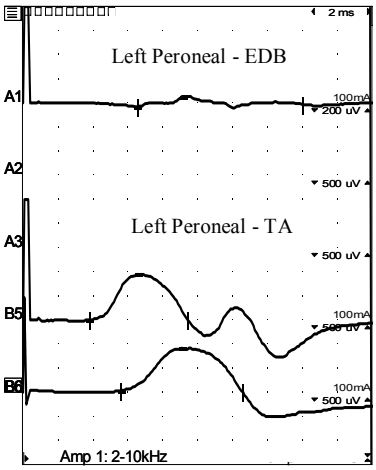

Right Tibial
Amp 1: 2-10kHz

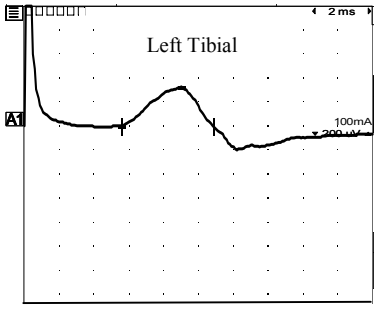

Right Median
Right Ulnar
Amp 1: 20-3kHz


Right Radial
Amp 1: 20-3kHz


Right Median
Amp 1: 2-10kHz


Right Ulnar
Amp 1: 2-10kHz


Left Peroneal - EDB
Left Peroneal - TA
Amp 1: 2-10kHz


Left Tibial

Bibliography –

Blum Andrew S. and Seward B. Rutkove, eds. The Clinical Neurophysiology Primer. Humana Press Inc. Totowa, New Jersey. 2007.

Daube, Jasper, ed. Clinical Neurophysiology. F.A. Davis Company, Philadelphia. 1996.

Dumitru, Daniel, Anthony Amato and Machiel Zwarts. Electrodiagnostic Medicine, 2nd Ed. Hanley and Belfus, Philadalephia. 2002.

England, J. D., MD, et al. eds. "Evaluation of Distal Symmetric Polyneuropathy: the Role of Autonomic Testing, Nerve Biopsy and Skin Biopsy (An Evidence-Based Review)." AANEM Practice Parameter, Muscle and Nerve. January 2009.

Feldman, Eva L. Clinical Manifestations and Diagnosis of Diabetic Polyneuropathy. Up-to-Date Online, 17.3. July 24, 2009.
http://www.utdol.com/online/content/topic.do?topicKey=Clinical manifestations and diagnosis of diabetic polyneuropathy

Kimura, Jun. Electrodiagnosis in Diseases of the Nerve and Muscle, Principles and Practice. 3rd Ed. Oxford, New York, Philadelphia. 2001.

Oh, Shin. Clinical Electromyography: Nerve Conduction Studies. 2nd Ed. Williams and Wilkins, Baltimore. 1993.

Preston, David and Barbara Shapiro. Electromyography and Neuromuscular Disorders; Clinical-Electrophysiologic Correlations. 2nd Ed. Elsevier, Philadelphia. 2005.

Rutkove, Seward B. Overview of Polyneuropathy. Up-to-Date Online, 17.3. February 9, 2009.
http://www.utdol.com/online/content/topic.do?topicKey=Overview of polyneuropathy.