Electrodiagnosis in Diabetic Neuropathies

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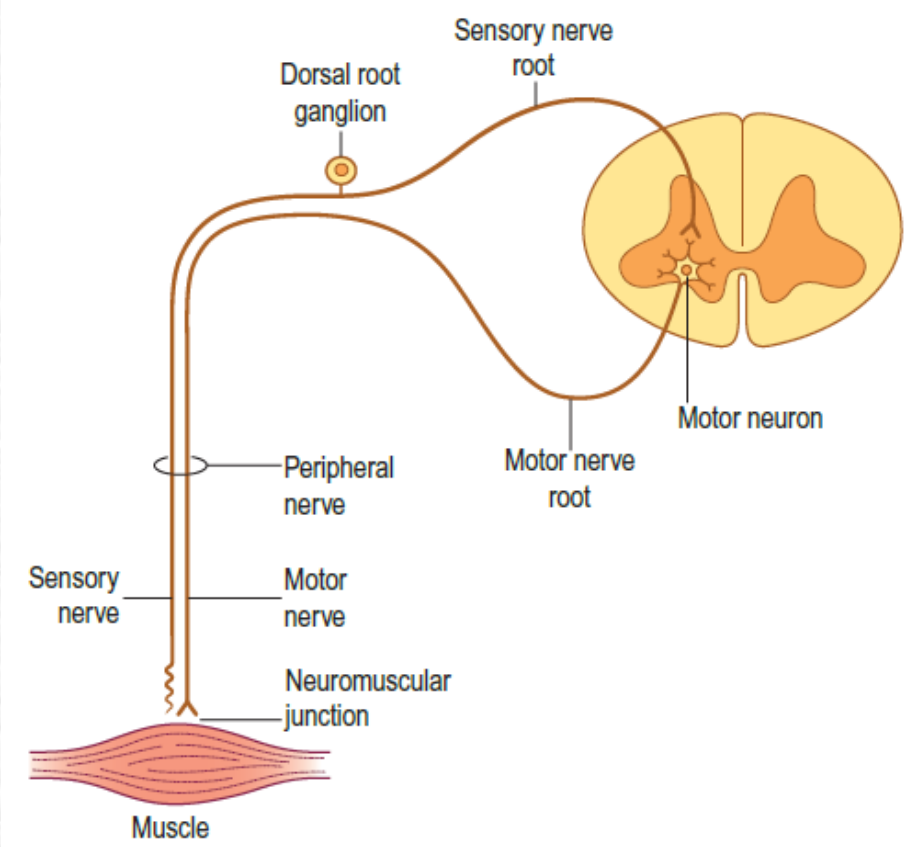
Electrodiagnostic medicine

- To evaluate peripheral neuromuscular system
- An extension of patient history and physical examination
- Measure the electrical properties of neuromuscular function
- Confirming a suspected diagnosis
- Excluding other possible diagnosis
- Identifying subclinical disease
- localizing abnormalities
- Defining disease severity
- Defining pathophysiology
- Defining disease evolution and guiding prognosis and treatment options

EDX Indications

- 1. A patient is complaining of numbness.
- 2. A patient is complaining of tingling (paresthesias).
- 3. A patient has pain.
- 4. A patient has weakness.
- 5. A patient has a limp.
- 6. A patient has muscle atrophy.
- 7. A patient has depressed deep tendon reflexes.
- 8. A patient has fatigue.

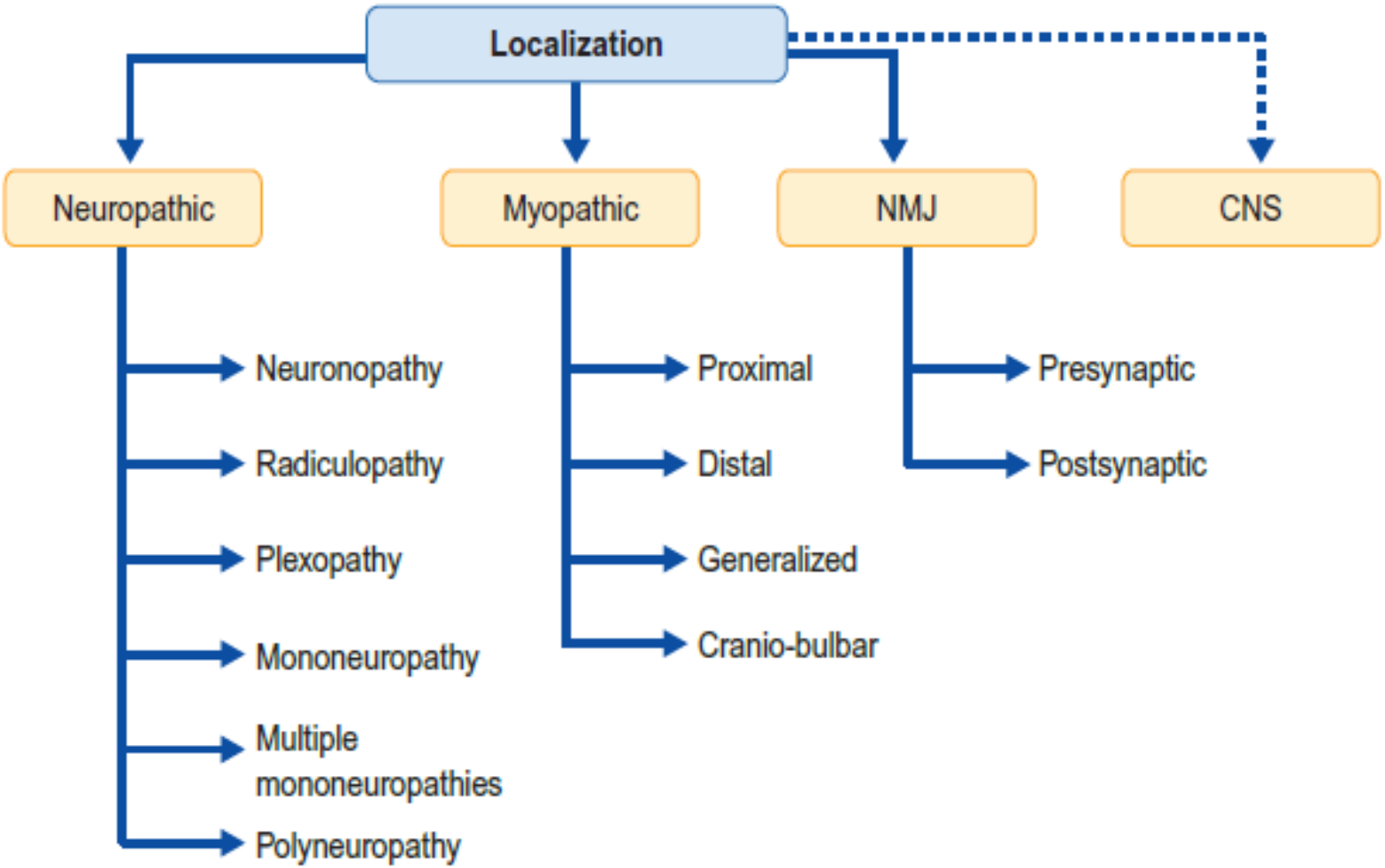
Peripheral Nerves System Disease



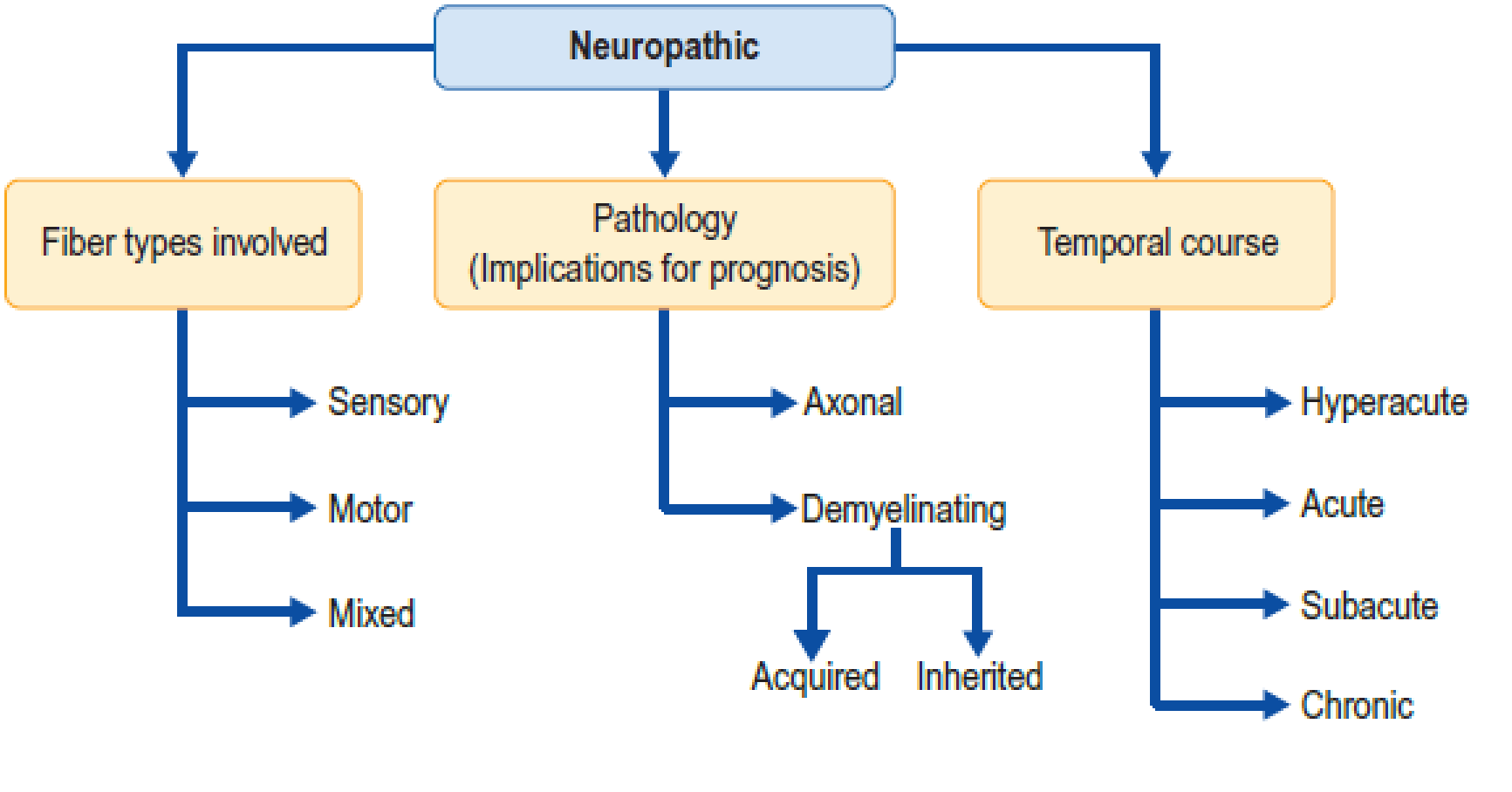
Box 1–1. Disorders of the Peripheral Nervous System

- Motor neuronopathy
  - Amyotrophic lateral sclerosis
  - Spinal muscular atrophy
  - Infectious (poliomyelitis, West Nile virus)
  - Monomelic amyotrophy
- Sensory neuronopathy
  - Paraneoplastic
  - Autoimmune
  - Toxic
  - Infectious
- Radiculopathy
  - Disk herniation
  - Spondylosis
  - Neoplastic
  - Infarction
  - Infectious
  - Inflammatory
- Plexopathy
  - Radiation induced
  - Neoplastic
  - Entrapment
  - Diabetic
  - Hemorrhagic
  - Inflammatory
- Neuropathy
  - Entrapment
  - Polyneuropathy
    - Demyelinating
    - Axonal
  - Mononeuritis multiplex
- Neuromuscular junction disorders
  - Myasthenia gravis
  - Lambert–Eaton myasthenic syndrome
  - Botulism
  - Toxic
  - Congenital
- Myopathy
  - Inherited
    - Muscular dystrophy
    - Congenital
    - Metabolic
  - Acquired
    - Inflammatory
    - Toxic
    - Endocrine
    - Infectious

Localization in PNS



Neuropathic



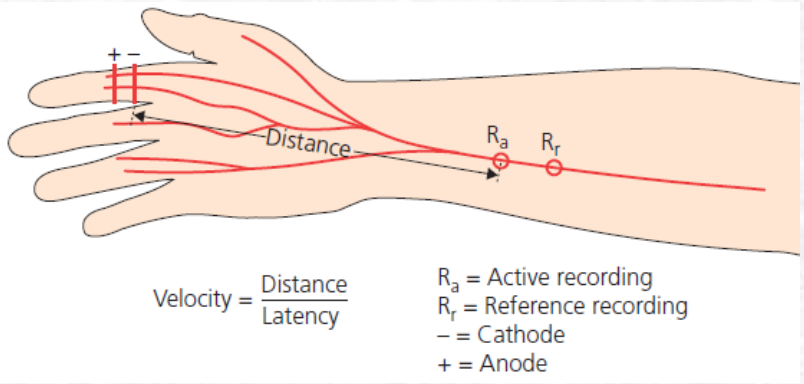
Electrodiagnostic Tests

- NCSs/Nerve Conduction Studies
- EMG/ Electromyography
- Late responses/F Wave H reflex
- RNS /Repetitive stimulation

Conduction Studies

- SNAP/Sensory Nerve Action Potential
- CMAP/ Compound Muscle Action Potential

SNAP



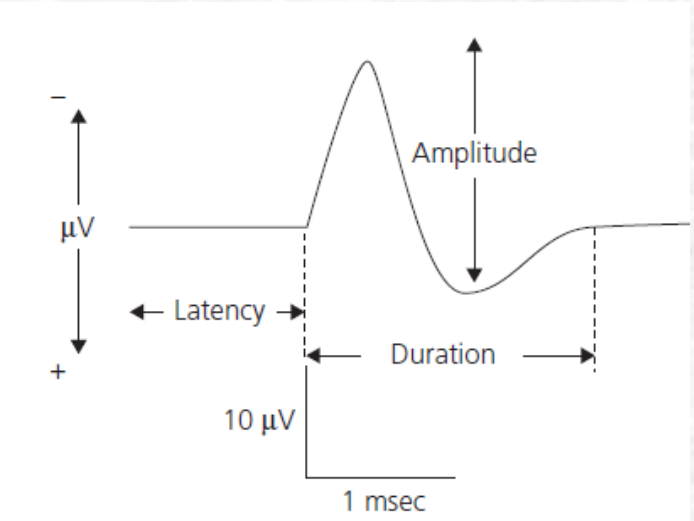


Figure 2.3 Measurement of the compound sensory nerve action potential (SNAP). Note the neurophysiological convention that upwards deflection is negative. Unfortunately there is not international uniformity of measurement parameters. Some laboratories will record orthodromic sensory responses measuring latency to initial waveform deflection from baseline, and peak-to-peak measurement for amplitude (shown in the figure). Others will record antidromic responses, latency to the negative peak and use baseline to negative peak amplitude measurements.

CMAP

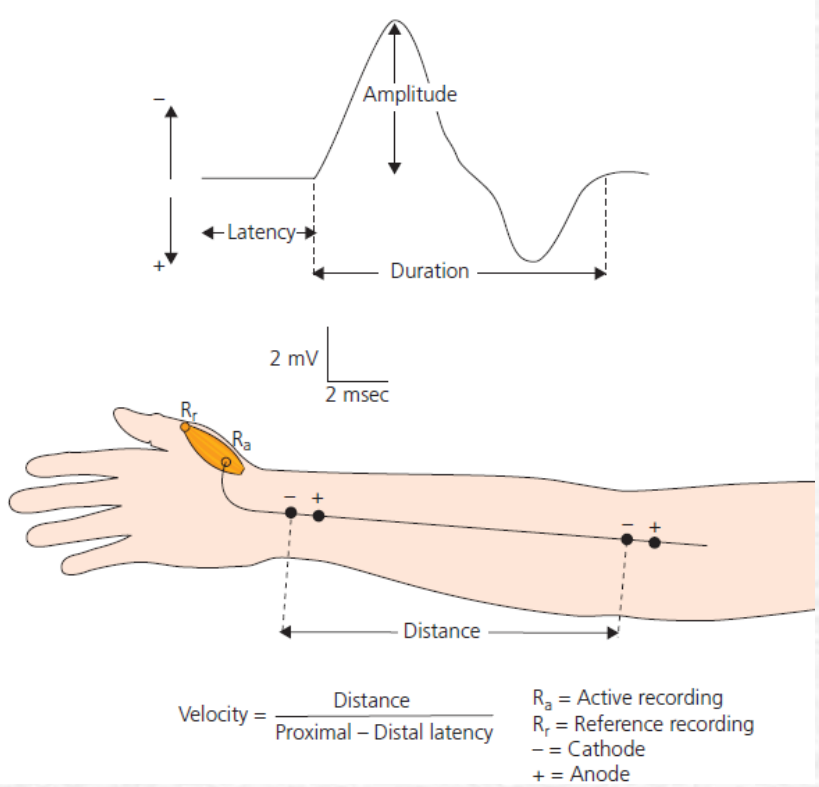


Figure 2.4 Measurement of the compound muscle action potential (CMAP). Note the neurophysiological convention that upwards deflection is negative. Latency is measured to the initial waveform deflection from baseline, and amplitude is from baseline to negative peak (check local practice).

CMAP/SNAP

Table 2.1 Comparison of sensory and motor nerve conduction measurements

	Sensory, SNAP	**Motor, CMAP**
Activity recorded	Nerve	Muscle
Amplitude	μV, peak to trough (check local practice)	mV, negative peak only
Duration	1–2ms	5–15ms
Velocity	Single site stimulation	Requires two sites of stimulation

Conduction Abnormalities

Axonal loss

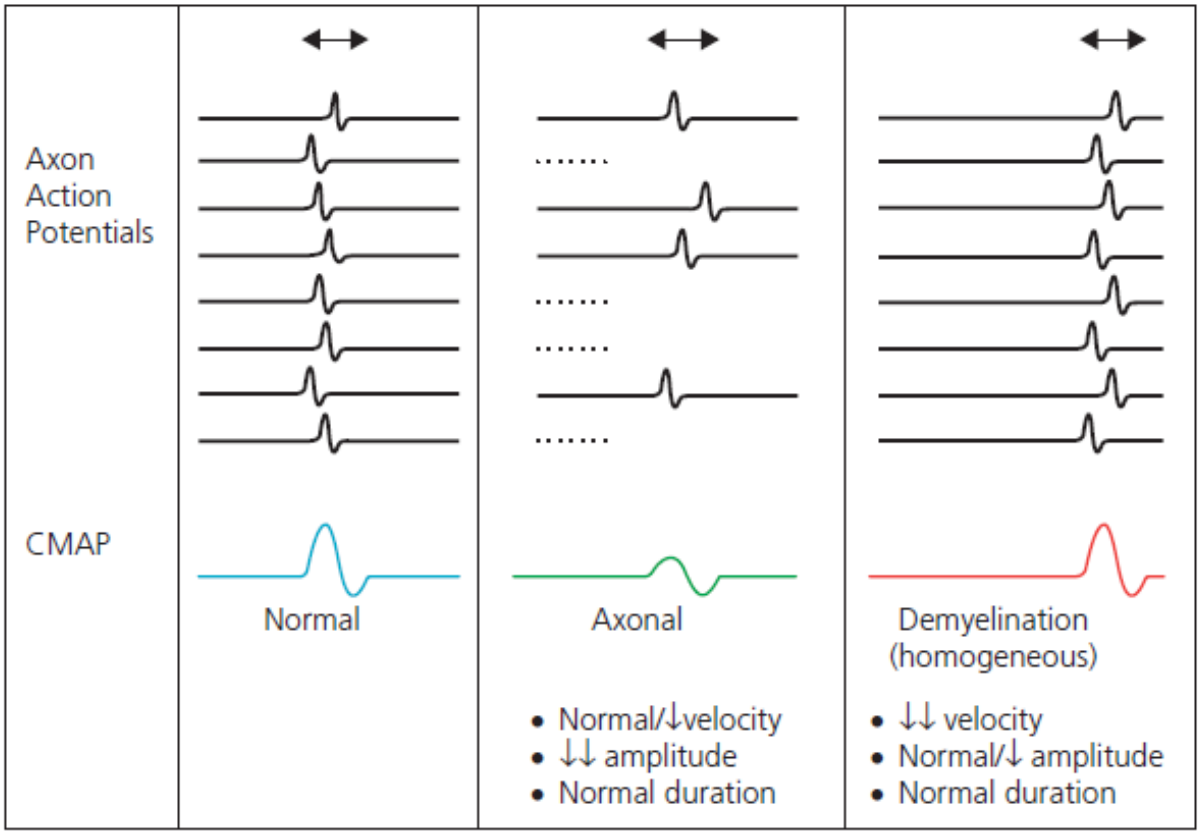


Figure 3.1 Nerve conduction with axonal versus demyelinating pathology. Compound muscle action potential (CMAP)–the sum of individual muscle fibre action potentials. With axon loss the summed amplitude is small, and with demyelination the nerve conduction velocity is usually slowed.

Demylinating

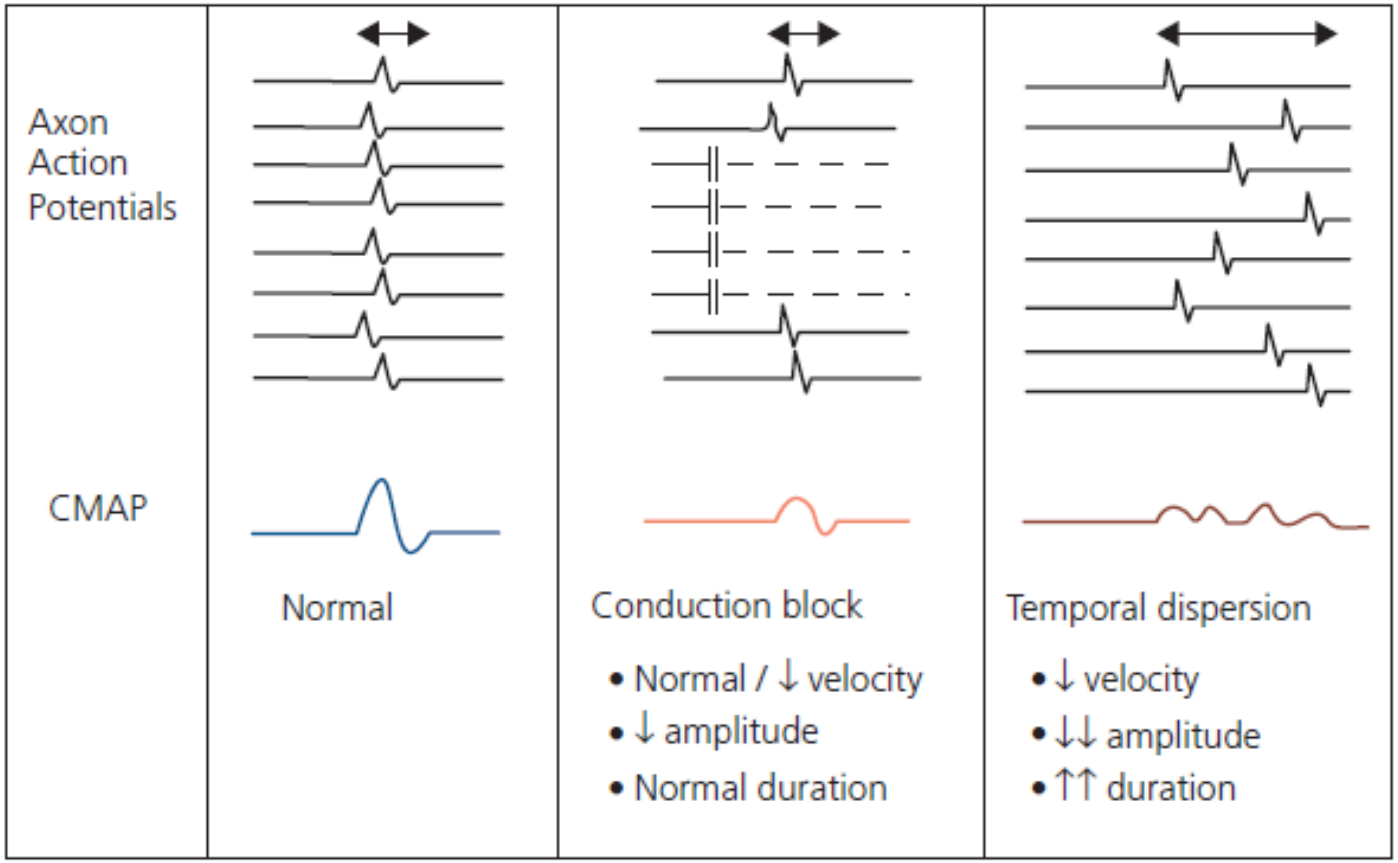


Figure 3.3 Nerve conduction studies with conduction block versus temporal dispersion. Stimulation above the site of partial conduction block results in a low amplitude but normal duration CMAP. With temporal dispersion the amplitude is also reduced, but the duration of the response is prolonged.

Nerve Regeneration after Axonal Injury

- Weeks: distal motor unit remodeling
- Months: regrowth of motor axons

Distal Motor Unit Remodeling

- The remodelling of surviving motor units (if there are any) starts with sprouting of new terminal branches of motor axons to contact nearby denervated muscle fibers, thus increasing the size of surviving motor units.

Regrowth

- Provided the nerve injury did not completely section the endoneurium,
- regrowth of axons from the proximal nerve stump begins soon after injury
- proceeds at about 1–2mm/day.
- The first regenerating axons initially reinnervate just one or two muscle fibers ‘nascent units’.

COMPONENTS OF THE ACTION POTENTIAL

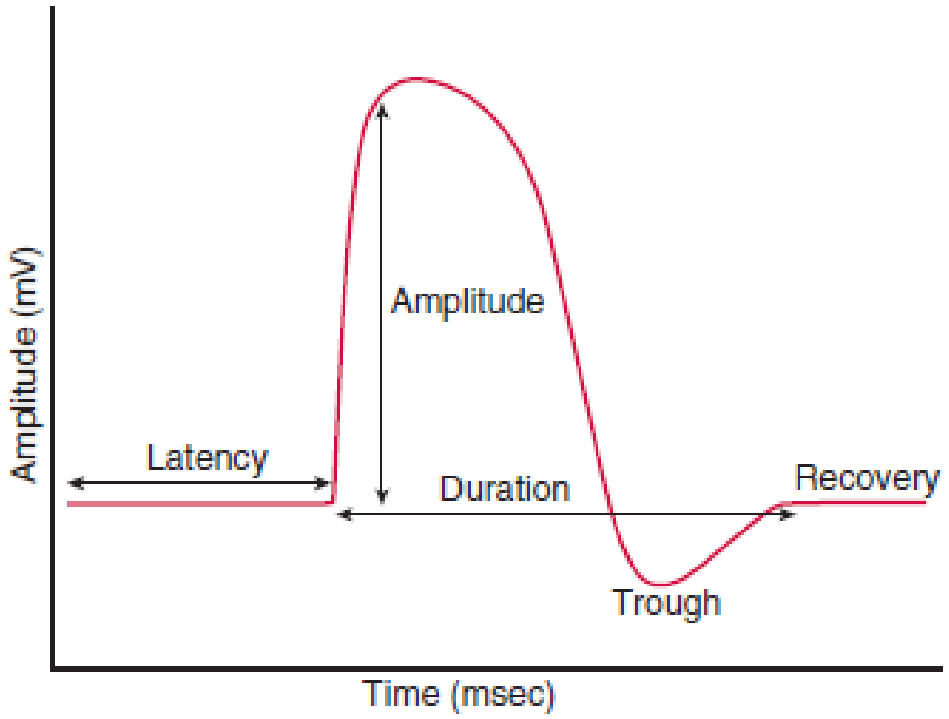


Figure 4.4 Compound muscle action potential.

Latency

- The latency represents the time it takes from stimulation of the nerve to the beginning of the SNAP or the CMAP.
- In a CMAP, the onset latency represents the arrival time (at the recording electrode over the muscle) of the fastest-conducting nerve fibers.
- In sensory nerves, the latency is solely dependent on the speed of conduction of the fastest fibers and the distance the wave of depolarization travels.
- In motor nerves, in addition to the speed of the nerve and the distance traveled, the latency is also dependent on the amount of time it takes to synapse at the neuromuscular junction and the speed of intramuscular conduction.
- Usually the latency is measured to the negative (upward) departure from baseline. If an initial positive departure is seen, the electrodes usually require repositioning, because it is likely that the recording electrode is over a muscle not innervated by the nerve being stimulated.
- It must be stressed that a latency measurement without a standardized or recorded distance is meaningless.

Conduction Velocity

- Conduction velocity is how fast the nerve is propagating an action potential.
- It can be calculated by the formula: velocity = distance/time
- Sensory nerves do not have a myoneural junction. Therefore, conduction velocity can be calculated directly by measuring the time it takes (in milliseconds) for the propagated action potential to travel the measured distance (in centimeters).
- Because motor nerves do conduct across a myoneural junction, the conduction velocity cannot be measured directly. Therefore, we use the formula: velocity = change in distance/change in time
- At least two sites must be stimulated. The difference in distance from the two stimulation sites is then divided by the difference in latencies of the two action potentials obtained.
- **Normal conduction velocities average**
- above 50 m/sec in the upper extremities
- above 40 m/sec in the lower extremities

Amplitude

- The amplitude of a CMAP represents the sum of the amplitudes of individual potentials.
- These individual potentials are generated by muscle fibers that are depolarized by nerve fiber axons of similar conduction velocities.
- The amplitude is therefore dependent on the integrity of the axons, the muscle fibers it depolarizes, and on the extent of variability of the conduction velocity of individual fibers.
- If some fibers are slow and others are fast, the action potential will be of longer duration (temporal dispersion) and lower amplitude .
- When there is a CMAP with low amplitude, it is important to distinguish whether this is occurring because of temporal dispersion or is due to a decreased number of axons .
- The total area under the curve gives a better indication of the number of axons or muscle fibers depolarized than the amplitude itself, especially in cases of temporal dispersion.

Duration

- The duration is the time from the onset latency to the termination latency/ time from departure from baseline to final return to baseline
- In some demyelinating diseases with nerve fibers affected differently, the duration may be increased (temporal dispersion).

Needle Electromyography

Needle electrode examination

- Is performed by inserting a needle electrode into a muscle and assessing its activity at rest , its response to small movements of the needle, and the activity on volitional contraction
- Its performance and interpretation comes only with experience
- Electromyographic (EMG) testing involves evaluation of the electrical activity of a muscle and is one of the fundamental parts of the electrodiagnostic medical consultation.

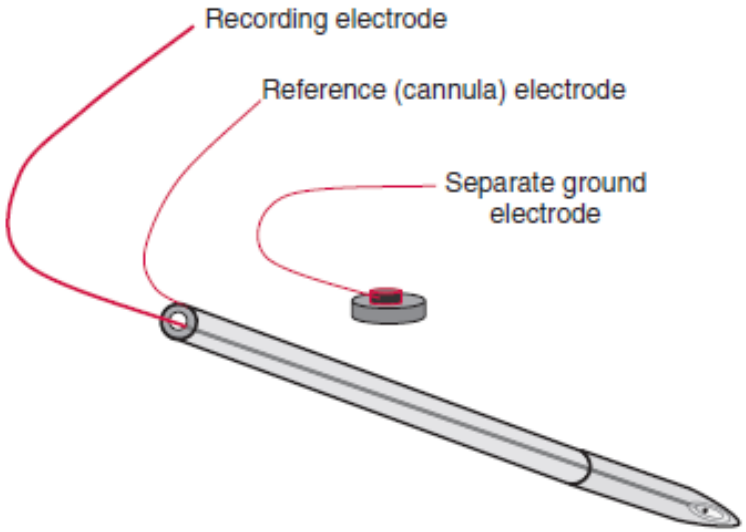
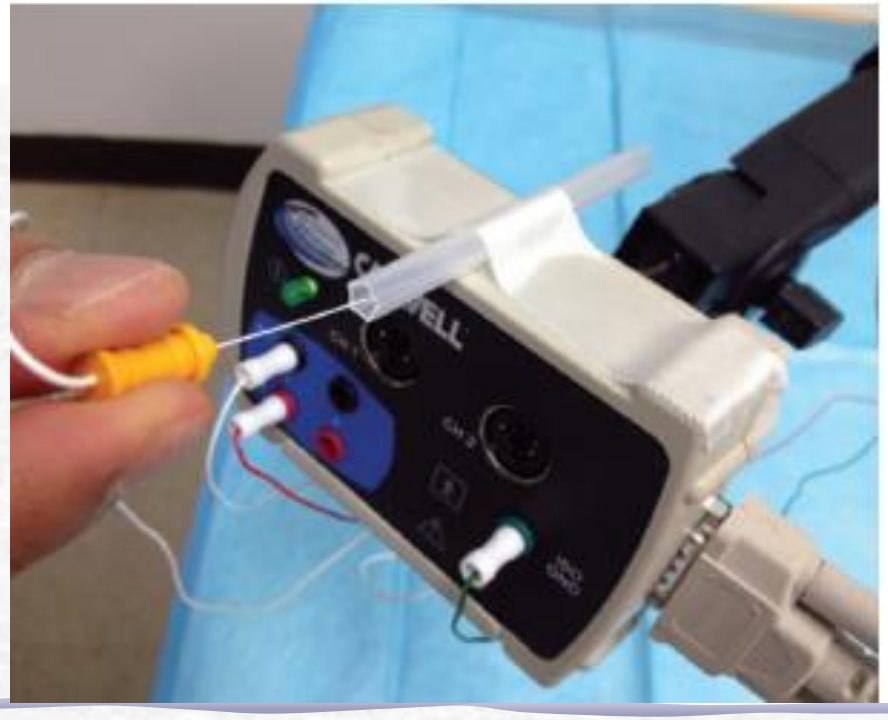


Figure 5.3 Concentric needle.



EMG examination

- insertional activity
- examination of the muscle at rest
- analysis of the motor unit
- recruitment

Insertional Activity

Insertional Activity

- brief burst of muscle depolarization after quick movement of needle
- 4-6 brief needle movement is necessary for assessment
- Increase IA=longer than 300 ms- in neuropathic and myopathic process
- Decrease IA=I replacement of muscles with fat or fibrous connective tissues

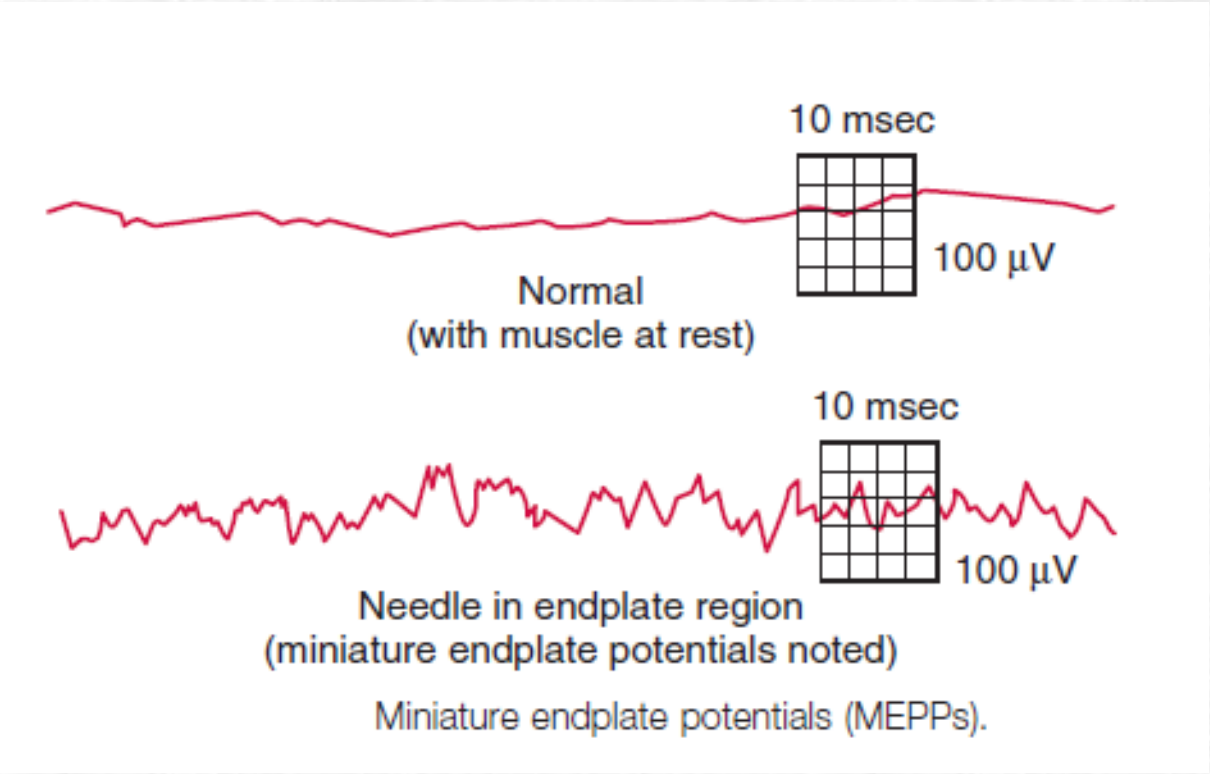
Spontaneous Activity

Spontaneous activity

- **Normal :**
- Endplate noise
- Endplate spikes
- **Abnormal:**
- Fibrillations Potentials
- Positive sharp wave
- Myotonic discharges
- Complex repetitive discharges
- **Abnormal motor unit potentials :**
- Fasciculation myokymic discharges
- Cramps

Endplate Noise

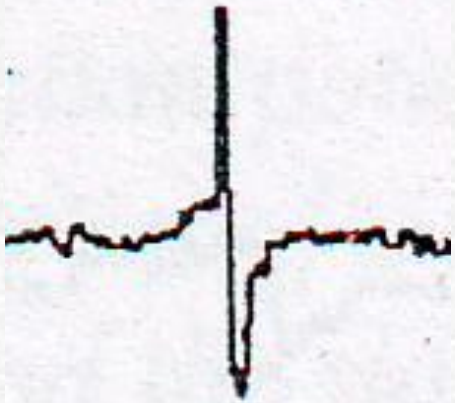
- Low amplitude monophasic negative potentials
- 20-40 Hz irregular firing
- Seashell sound



Miniature endplate potentials (MEPPs).

Endplate Spike

- MFAPs that fire irregularly up to 50 Hz
- Along with endplate noise
- Biphasic with initial negative deflection
- Cracking sound
- As result of needle induced irritation of a terminal nerve twig

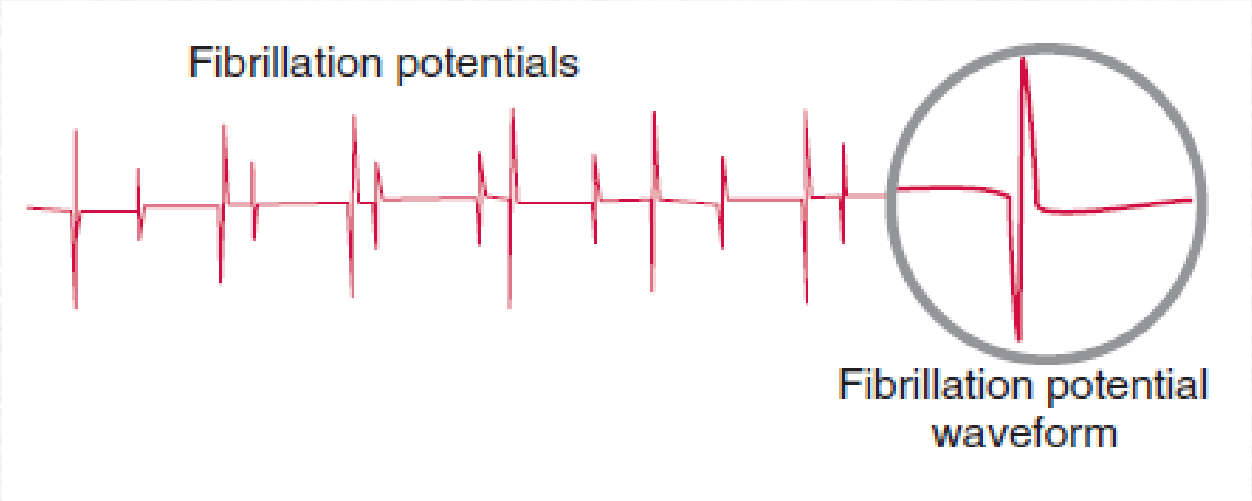


Spontaneous Activity
Abnormal muscle fiber potentials

- Any persistent spontaneous activity out of the endplate zone , usually longer than 3 seconds
- Fibrillation potentials
- Positive Sharp Waves, PSW
- Complex repetitive discharges, CRD
- Myotonic Discharges

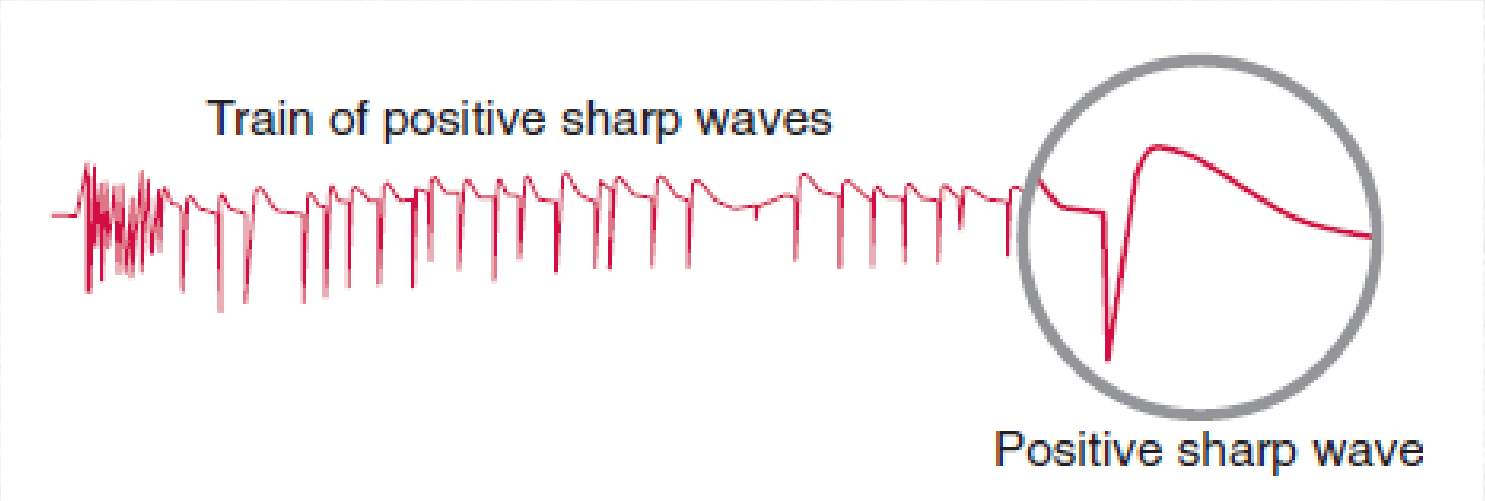
Fibrillation Potentials

- From extracellular recording of a single muscle fiber
- Marker of active denervation
- Single muscle fiber action potentials, MFAP
- A brief spike with initial positive deflection
- 1-5 ms duration , low amplitude 10-100 micro V
- Regular firing at rate of 0.5 to 10 Hz
- Sound like rain on the roof



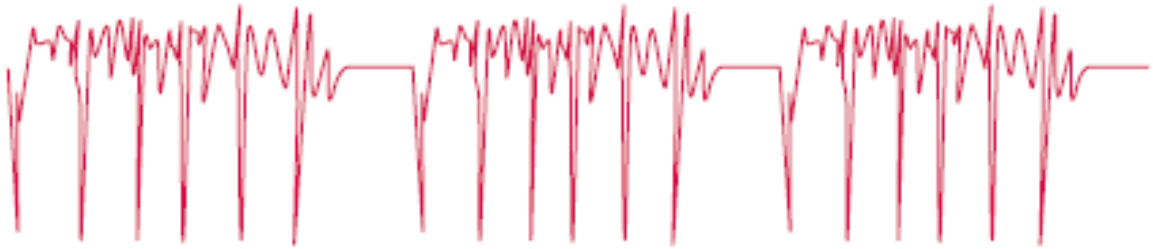
Positive Sharp Wave

- same significance as fibrillation potentialls
- A brief initial positivity followed by a long negative phase
- Sound like a dull pop
- Amp 10-100 micro V
- Regular firing at 0.5 to 10 Hz



Complex Repetitive Discharges

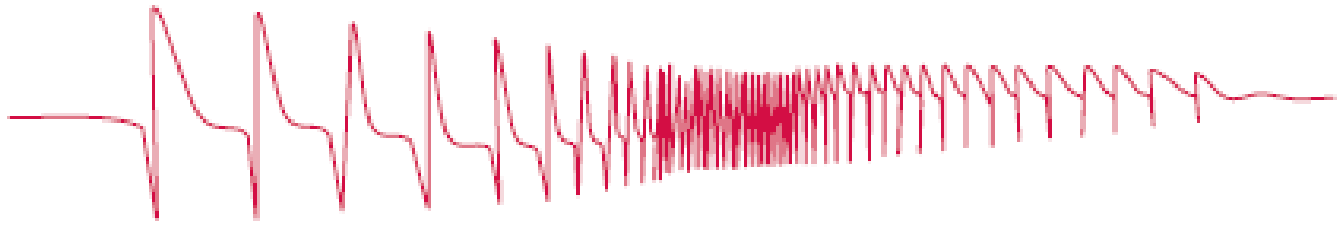
- From depolarization of a single muscle fiber followed by ephaptic spread to adjacent denervated fibers
- High frequency(20-150) multiserrated repetitive discharges with an abrupt onset and termination
- In chronic neuropathic and sometimes chronic myopathic disorders
- Spontaneous or following needle movement
- Sound machine



Complex repetitive discharge.

Myotonic Discharges

- Spontaneous discharge of muscle fiber
- Waxing and waning of both amplitude and frequency
- Firing rate: 20-150 Hz
- Either a positive wave or a brief spike morphology
- Revving engine sound



Myotonic discharges. Note waxing and waning in frequency and amplitude.

Spontaneous Activity
Abnormal Motor Unit Potentials

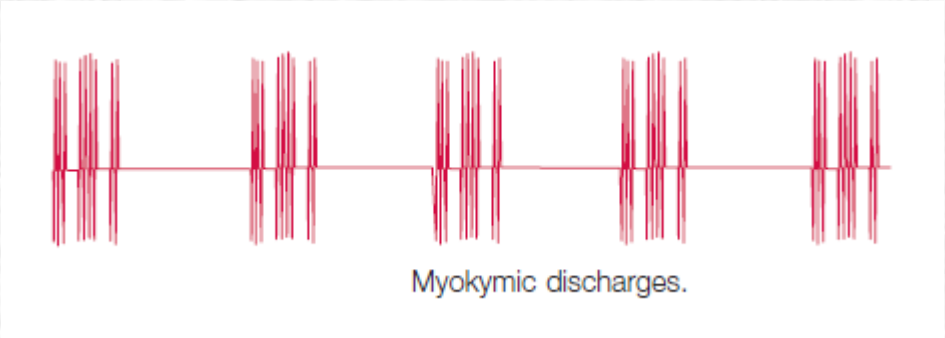
- Fasciculation potentials
- Myokymic Discharges

Fasiculation Potentials

- Single , spontaneous , involuntary discharge of an individual motor unit
- Slow firing , less than 1-2 Hz and irregular(voluntary MUAPs firing at 4-5 Hz)

Myokymic Discharges

- Rhythmic , grouped, spontaneous repetitive discharges of the same motor unit(grouped fasciculations)
- Firing frequency within the burst typically is 5-60 Hz
- Firing frequency between bursts is much slower (less than 2Hz)
- Marching sound

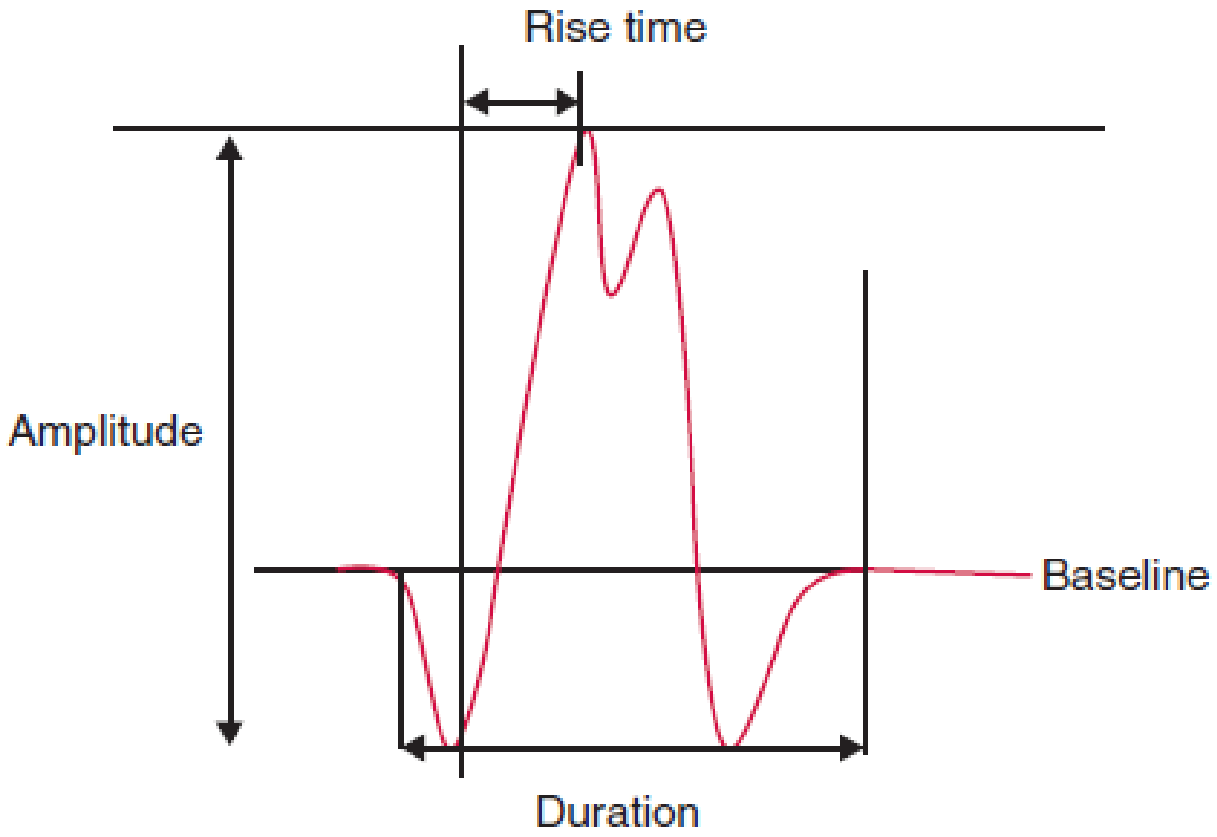


Myokymic discharges.

Analyzing (MUAP)

- Once the muscle has been assessed for insertional activity and activity at rest, the motor unit itself should be analyzed.
- During this portion of the needle test, the patient is asked to minimally contract the muscle.
- When analyzing motor units, the sweep speed should be set at 10 msec per division and the gain should be 500–1000 mV per division.

MUAP Parameters



Motor Unit Action Potential (MUAP) components.

Evaluation of motor unit action potentials

- Morphology :
- - duration
- - amplitude
- - phases
- Stability
- Firing characteristics (Recruitment)

Amplitude of MUAP

- Muscle fibers located near the tip of the electrode make the greatest contribution to the amplitude of the motor unit potential.
- Measured from peak to peak of motor unit
- MUAP amplitude is measured from the most positive to the most negative peak, and it reflects fiber density.
- Mostly grater than 100 microvolt and less than 2 milivolt
- Varies widely among normal subjects
- Reflects only those few fibers nearest to the needle(2-12 fibers)
- Not helpful as duration in judging motor unit size
- Amplitudes are larger with a monopolar needle (normally 1–7 mV) because the monopolar needle picks up electrical activity from a full 360-degree field around the needle

Amplitude increases

- 1) as the needle approximates the MU;
- 2) as you increase the number of muscle fibers of the MU;
- 3) with increasing diameter of the muscle fibers (muscle fiber hypertrophy);
- 4) with more synchronous firing of the muscle fibers.

Rise Time

- the time lag from the initial positive deflection to the subsequent negative upward peak.
- To estimate the distance between the recording tip and discharging motor unit
- The more vertical the waveform, the shorter (quicker) the rise time.
- A distant motor unit has longer rise time because the resistance and capacitance of the intervening tissue act as high-frequency filters
- A unit accepted for qualitative measurement should produce a sharp sound, while a distant unit will produce a dull sound indicating the need to reposition the needle electrode closer to the source.
- An acceptable rise time is 0.5 msec or less.

Duration of MUAP

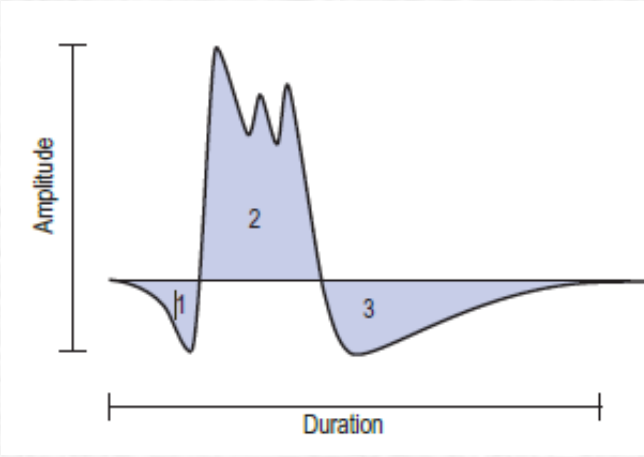
- It indicates the degree of synchrony of firing among all individual muscle fibers with variable lengths, conduction velocities, and membrane excitabilities.
- When all the fibers of a motor unit fire in relative synchrony, the duration will be short.
- If there is asynchrony of firing (for example, with reinnervation), the duration will be longer.
- A slight shift in the needle position influences the duration much less than the amplitude.
- From the initial deflection from baseline to the final return of the MUAP to baseline
- Primarily depends on the number of muscle fibers within the motor unit
- Proximal and bulbofacial muscles in general have shorter duration MUAP

Duration of MUAP C

- Increased age; Increased duration
- Decreased temperature; Increased duration
- Typical MUAP duration is between 5-15 ms
- Sound: long-duration=low frequency=dull
- Sound: short-duration=higher frequencies=crisp
- Increased duration is seen in neuropathic processes, while decreased duration is seen in myopathic disorders.
- Duration is decreased in myopathies because fewer muscle fibers contribute to the motor unit.

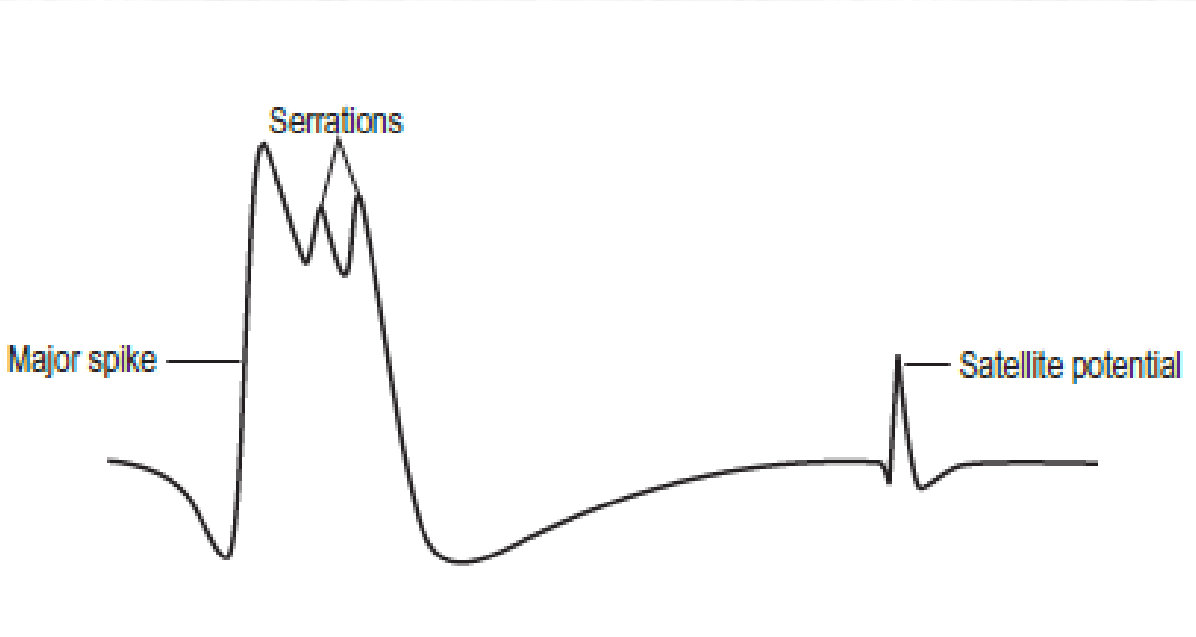
Phases /Polyphaisa

- Number of phases=number of baseline crossing +1/ counting negative and positive peaks
- Normal= 2-4 phases
- Polyphasic motor units (more than four phases) suggest desynchronized discharge or drop-off of individual fibers.
- Normal muscles may have up to 15% polyphasic MUAPs when using a concentric needle and up to 30% polyphasic MUAPs when using a monopolar needle.
- May be abnormal in both neuropathic and myopathic disorders
- Sound; high frequency clicking sound
- polyphasia= a measure of synchrony , that is , the extent to which the muscle fibers within a motor unit fire more or less at the same time



Serrations/Turn

- Changes in the direction of the potential that do not cross the baseline
- Increased polyphasia and serrations have similar implications
- Indicating less synchronous firing of muscle fibers within a motor unit



Motor Unit Stability

- Stable in morphology from potential to potential (changes in amplitude or number of phases)
- Normal effective transmission across the NMJs and all muscle fibers of the motor unit fire
- Changes between potentials in amplitude or in number of phases
- In primary disorders of the neuromuscular junction (NMJ) or disorders associated with new or immature NMJs (reinnervation)/ as secondary phenomenon in both myopathic and neuropathic disorders

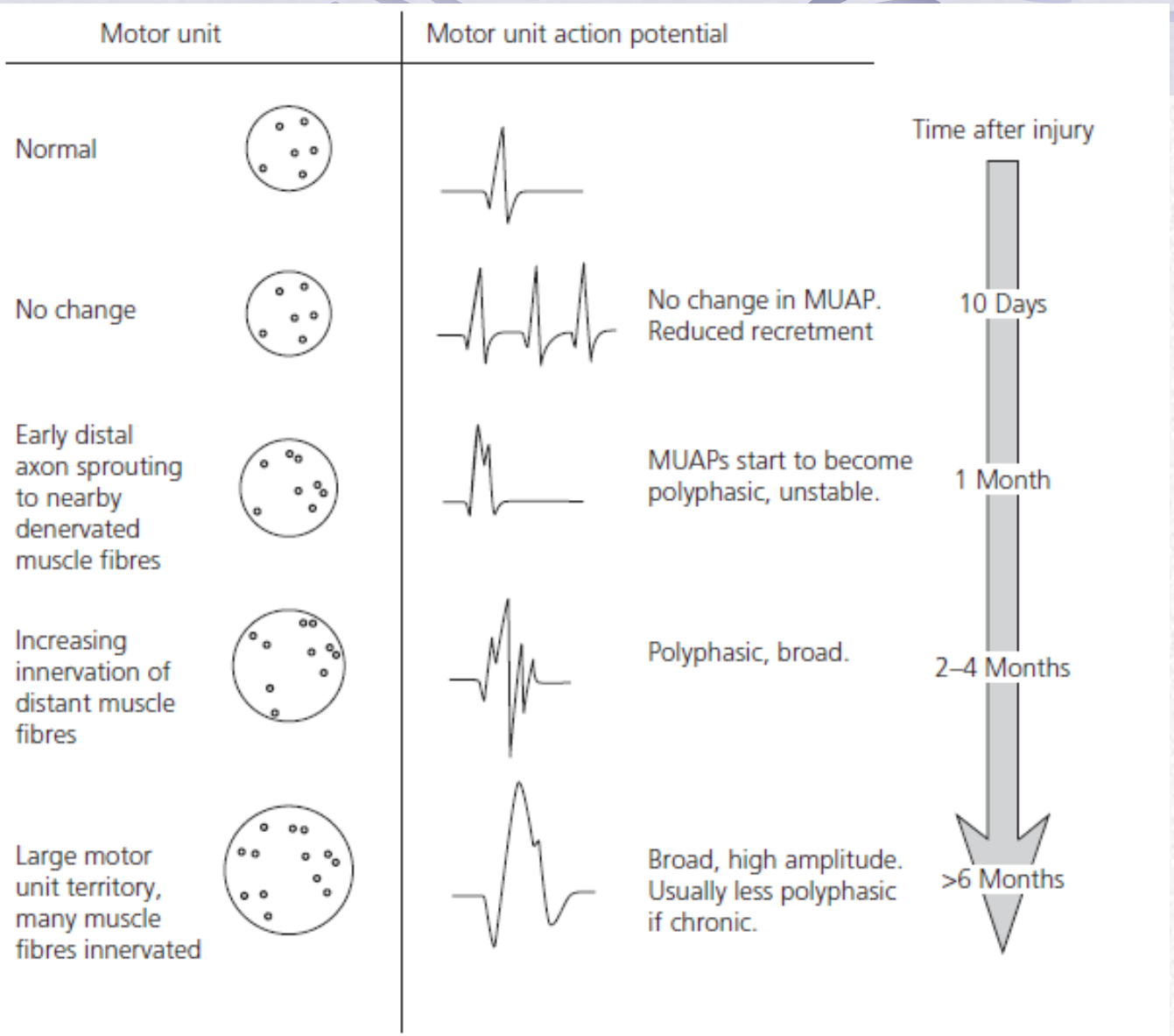


Figure 8.3 Motor unit action potential (MUAP) remodelling after partial axonal injury.

Recruitment Pattern

Recruitment

- Refers to the orderly addition of motor units so as to increase the force of a contraction.
- A contraction becomes stronger in two ways: the firing motor units increase their rate of firing and additional motor units commence firing.
- The machine settings : sweep of 10 msec per division and a gain of 500–1000 mV per division.
- Recruitment analysis should begin with the patient being told to think about contracting the muscle being analyzed.

Normal Recruitment Pattern

- Normally the motor unit will fire in a regular pattern at about 5 Hz.
- At around 10 Hz, another MUAP will be recruited to fire. The new MU will initially fire at about 5 Hz.
- The normal firing rate of most motor units, before additional units are recruited, is 10 Hz.
- To calculate the firing rate of the MU, note how many times an MU with an identical morphology repeats across a screen set at 100 msec per screen (sweep speed of 10 msec per division). Multiply that number by ten to get the motor unit firing per 1000 msec or 1 s. Remember that Hz indicates cycles per second.

A-1	B-2	C-3	D-4
5			
10	5		
15	10	5	
20	15	10	5

Recruitment Abnormalities

- Decreased:
- - Loss of MUAPs
- Decreased activation:
- - Normal number of MU/ in uncooperative state, pain , CNS problems
- Early or easy recruitment:
- - Dropout individual muscle fibers from a motor unit , inappropriate firing of many motor units to generate a small amount of force

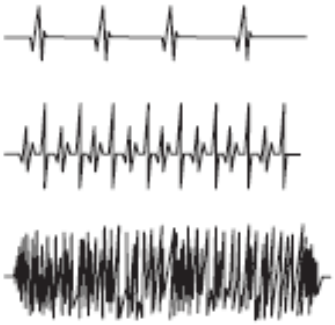
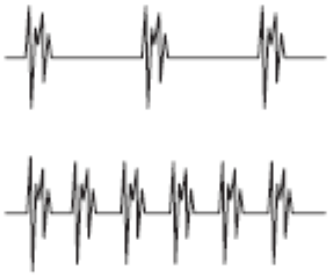
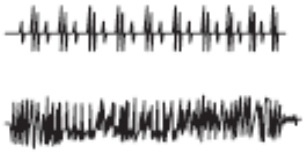
In a neuropathic process

- Only some motor units will be unavailable to fire
- A motor unit that is able to fire will try to 'make up for' the inability of other units to fire by firing at a higher frequency.
- Therefore, the motor unit will have an increased firing frequency before another motor unit is recruited, which is referred to as decreased recruitment.
- In decreased recruitment, there are fewer motor units firing at higher frequency
- can be seen in neuropathies, radiculopathies, motor neuron disease, and trauma
- The firing rates of these MUAPs are greater than 20 Hz (20 cycles per second) and may increase to 30 Hz or more.
- If only a few motor units are firing but they are firing at a normal rate,
- recruitment is normal. The decreased activation of the muscle may be due to either decreased effort or to a central nervous system lesion.

Myopathic process

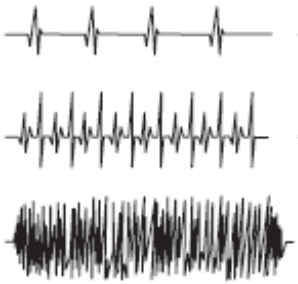
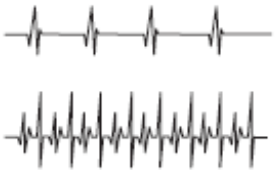
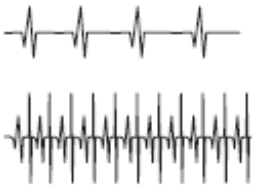
- increased recruitment and early recruitment
- In myopathic recruitment, a large number of motor units are recruited for a minimal contraction.
- In myopathies, the individual muscle-fiber contribution to each motor unit is reduced .
- Because myopathic fibers cannot increase their force outputs, they quickly recruit additional motor units to increase the force of a contraction
- In this situation, one motor unit will fire at only about 5 Hz before the next motor unit is recruited.

Table 5.5 Recruitment pattern with abnormal motor units, normal central drive

	Normal	Neurogenic	Myopathic
Number of motor units	N	↓	N
Size of motor units	N	↑	↓
Central drive	N	N	N
Recruitment	*Normal*: orderly activation of progressively larger motor units to a full interference pattern with strong contraction	*Reduced*: with maximal effort only few motor units fire, but they do so at high rates (in a weak muscle)	*Rapid/early*: with weak contraction many more motor units are active than normal since they are individually weak (as is muscle strength)
Weak contraction ↓ Strong contraction			
Interference pattern	N	↓	Full, but low amplitude

N, normal; ↓, decreased; ↑, increased.

Table 5.6 Recruitment pattern with abnormal central drive, normal motor units

	Normal	**Upper motor neuron lesion, pain, volitional**	**Peripheral conduction block**
Number of motor units	N	N	N, but only a fraction can be activated
Size of motor units	N	N	N
Central drive	N	↓	N
Recruitment	*Normal*: orderly activation of progressively larger motor units to a full interference pattern with strong contraction	*Poor activation*: recruitment is initially normal, but full activation is not achieved. Firing rate is normal for the number of motor units active and the low force of contraction	*Reduced*: with maximal effort only few motor units fire, but they do so at high rates (in a weak muscle)
Weak contraction ↓ Strong contraction			
Interference pattern	N	↓	↓

N, normal; ↓, decreased.

Interference pattern

Interference Pattern

- Result of maximal exertion.
- Achieving a full interference pattern requires both adequate central drive and a normal number of motor units.
- **Attention to:** The degree of obliteration of the baseline of the record, and the amplitude of the interference pattern.
- This is rather less susceptible to needle movement than the amplitude of single motor unit action potentials since it is determined by many such potentials.
- Patients with peripheral motor conduction block or a lack of central drive will have a reduced interference pattern but they may be told apart by the recruitment and firing patterns already discussed, and of course their different clinical presentation.

Neurogenic Interference Pattern

- The interference pattern is reduced,
- abnormally high amplitude, polyphasic, long-duration motor unit action potentials
- Firing at high rates but with appreciable brief gaps in between them.
- Very characteristic juddering sound.

Abnormal MUAP Patterns

Neuropathic Pattern

- **Acute axonal loss:**
- Normal morphology of MUAP-Decreased recruitment pattern
- **Chronic axonal loss:**
- MUAP changes as high amplitude, long duration and polyphasic
- **Demyelinating:**
- Normal MUAP morphology-Decresed recruitment

Myopathic Pattern

- **Acute :**
- short duration, small amplitude , polyphasic MUAPs- normal or early recruitment
- **Chronic:**
- both type of MUAPs mainly in the necrotic or inflammatory types-Normal or early recruitment, which is key for differentiating chronic myopathic as chronic neuropathic
- **End stage:**
- unusual pattern of reduced recruitment pattern with short duration, small amplitude , polyphasic MUAPs alone or in combination with long duration, high amplitude, polyphasic MUAPs

General EMG Pathologies

Peripheral Neurogenic Syndromes

Neurogenic entities	**Neuropathic findings distribution**
mononeuropthy	Limited to one nerve
Polyneuropathy:Stoking-Glove	Distal more than proximal Lower extremity more than upper Symmetric bilateral-length dependant
Polyneuropathy: Asymmetric Axonal	Asymmetric-Nonlength dependant Multiple mononeuropathies
Plexopathy	Multiple nerves of one plexus
Radiculopathy	Limited to one myotome Including the paraspinals
Polyradiculopathy	Multiple myotomes Including the paraspinals
Motor neuron Disease	Multiple myotomes Thoracic paraspinals Bulbar muscles

Diabetic Neuropathies

Diabetes Mellitus Related Neuropathies

- Distal symmetric sensory and sensorimotor polyneuropathy
- Autonomic neuropathy
- Diabetic neuropathic cachexia
- Polyradiculoplexus neuropathy
- Mononeuropathy/multiple mononeuropathies
- Acute treatment–induced painful neuropathy
- Hypoglycemia/Hyperinsulinem Generalized sensory or sensorimotor polyneuropathy

DIABETIC DISTAL SYMMETRIC SENSORY AND SENSORIMOTOR POLYNEUROPATHY (DSPN)

Clinical Features of DSPN

- The most common form of diabetic neuropathy.
- A length dependent neuropathy in which affected individuals develop sensory loss beginning in the toes, which gradually progresses over time up the legs and into the fingers and arms.
- When severe, a patient may also develop sensory loss in the trunk (chest and abdomen) in the midline that spreads out laterally toward the spine.
- Sensory loss is often accompanied by paresthesia, lancinating pains, burning, or a deep aching discomfort in 40–60% of patients with DSPN.
- A severe loss of sensation can lead to increased risk of infection, ulceration, and Charcot joints.
- Patients with **small fiber neuropathy** can also develop symptoms and signs of an autonomic dysfunction, as the autonomic nervous system is mediated by small myelinated and unmyelinated nerve fibers.
- Poor control of DM and the presence of nephropathy correlate with an increased risk of developing or worsening of DSPN.

Neurological examination

- reveals loss of small fiber function (pain and temperature sensation) only or panmodality sensory loss.
- Those individuals with large fiber sensory loss have reduced muscle stretch reflexes, particularly at the ankles, but reflexes can be normal in patients with only small fiber involvement or in patients whose neuropathy has not ascended far enough proximally to affect the reflex arc of the Achilles deep tendon reflex.
- Muscle strength and function are typically normal, although mild atrophy and weakness of foot intrinsics and ankle dorsiflexors may be detected.
- Because patients without motor symptoms or signs on clinical examination often still have electrophysiological evidence of subclinical motor involvement, the term “distal symmetric or length-dependent sensorimotor peripheral neuropathy” is also appropriate.

EDX

- Sensory NCS:
  Up to 50% of patients with DM have reduced sensory nerve action potential (SNAP) amplitudes and slow conduction velocities of the sural or plantar nerves
- Up to 80% of symptomatic individuals have abnormal sensory nerve conduction studies (NCS)
- Quantitative sensory testing:
- May reveal reduced vibratory and thermal perception
- Autonomic testing:
- May also be abnormal, in particular quantitative sweat testing.

- Motor NCS:
- Are less severely affected than the sensory studies but still are frequently abnormal with low amplitudes and normal or only slightly prolonged distal latencies and slow nerve conduction velocities (NCVs)
- **Rarely**, the NCV slowing can be within the "demyelinating range" (e.g., less than 30% below the lower limit of normal); however, conduction block and temporal dispersion are not usually appreciated
- EMG:
- May demonstrate fibrillation potentials, positive sharp waves, and large motor unit action potentials (MUAPs) in the distal muscles.

DIABETIC AUTONOMIC NEUROPATHY

Clinical Features

- Ttypically is seen in combination with DSPN and only rarely in isolation.
- Manifestations:
- abnormal sweating,
- dry feet,
- dysfunctional thermoregulation,
- dry eyes and mouth,
- pupillary abnormalities,
- cardiac arrhythmias,
- postural hypotension,
- gastrointestinal abnormalities (e.g., gastroparesis, postprandial bloating, chronic diarrhea, or constipation)
- genitourinary dysfunction (e.g., impotence, retrograde ejaculation, and incontinence).
- Important Note:
- The presence of autonomic neuropathy doubles the risk of mortality.

EDX

- Sensory and motor NCS:
- same features with DSPN
- Tests of autonomic function are generally abnormal, including:
- sympathetic skin responses

DIABETIC NEUROPATHIC CACHEXIA (DNC)

DNC - Clinical Features

- Very rare
- Can be the presenting manifestation of DM
- More common in men
- In men usually associated with type 2 DM
- In women in most cases associated with type 1 DM
- Generally occurs in their sixth or seventh decade of life
- Patients develop an abrupt onset of severe generalized painful paresthesias involving the trunk and all four limbs, usually setting off significant precipitous **weight loss**
- Mild sensory loss may be detected on examination along with reduced muscle stretch reflexes.
- Weakness and atrophy are evident in some patients.
- Tends to gradually improve spontaneously, usually preceded by recovery of the weight loss
- Rarely can recur

EDX

- **SNAPs:**
- May be absent or have very low amplitudes.
- **CMAPS:**
- Normal or slightly diminished amplitudes with mild slowing of conduction velocities
- **Needle EMG:**
- Evidence of active denervation in the form of fibrillation potentials and positive waves in affected muscles.

DIABETIC POLYRADICULOPATHY OR RADICULOPLEXUS NEUROPATHY

- Two categories :
- (1) the more common asymmetric**, painful**, radiculoplexus neuropathy (i.e., diabetic amyotrophy)
- (2) the rare symmetric, relatively **painless**, radiculoplexus neuropathy.
- - This form is controversial.
- - It may represent chronic inflammatory demyelinating polyneuropathy (CIDP) in a patient with diabetes, a distinct form of diabetic neuropathy, or may just fall within the spectrum of diabetic amyotrophy.

ASYMMETRIC, **PAINFUL** DIABETIC POLYRADICULOPATHY OR RADICULOPLEXUS NEUROPATHY (DIABETIC AMYOTROPHY)

Clinical Features

- Most common form of polyradiculopathy or radiculoplexus neuropathy associated with DM
- Also known as **diabetic amyotrophy**, Bruns–Garland syndrome, diabetic lumbosacral radiculoplexopathy, and proximal diabetic neuropathy
- More commonly affects older patients with DM type 2
- Can affect type 1 diabetic patients
- Can be the presenting manifestation of DM in approximately one third of patients.
- Typically, patients present with **severe pain** in the low back, hip, and thigh in one leg.
- Rarely, the diabetic polyradiculoneuropathy begins in both legs at the same time. Nevertheless, in such cases nerve involvement is generally asymmetric.
- 50% of patients also complain of numbness and paresthesia
- Atrophy and weakness of proximal and distal muscles in the affected leg become apparent within a few days or weeks.

Clinical Features

- The term **"proximal diabetic neuropathy"** stems from the observation that muscles innervated by the L2–L4 myotomes are the most commonly affected, producing weakness of hip flexion, hip adduction, and knee extension.
- The knee jerk on the affected side is virtually always diminished or lost in many cases.
- Any leg muscle may be affected

- May undergo unnecessary laminectomies because of incidental magnetic resonance imaging (MRI) findings in the presence of severe radicular pain and weakness suggesting structural impingement
- The onset is typically unilateral, it is not uncommon for the contralateral leg to become affected several weeks or months later.
- As with DNC, the polyradiculoneuropathy is often accompanied or heralded by severe weight loss.
- Weakness progresses gradually or in a stepwise fashion, usually over several weeks or months, but can continue to progress for 18 months or more
- Most patients usually have underlying DSPN.
- Eventually, the disorder stabilizes, and slow recovery ensues over 1–3 years.
- In many cases there is significant residual weakness, sensory loss, and pain.

- Rather than the more typical lumbosacral radiculoplexus neuropathy, some patients develop thoracic radiculopathy
- Patients describe pain radiating from the posterolateral chest wall anteriorly to the abdominal region, with associated loss of sensation anterolaterally.
- Weakness of the abdominal wall may lead to herniations of the viscera.
- A cervical variant of diabetic radicular plexus neuropathy manifesting as acute pain, weakness, and sensory loss in one or both upper limbs can rarely occur as well.

EDX

- NCS:
- Reveal features suggestive of multifocal axonal damage to the roots and plexus with reduced or low amplitudes of SNAPs and CMAPs.
- Conduction velocities in the affected limbs are normal or mildly slow.

Autonomic studies:

- may be abnormal

Needle EMG:

- Reveals positive sharp waves and fibrillation potentials and reduced recruitment of affected proximal and distal muscles in the affected limbs and paraspinal muscles in keeping with the radiculoplexus localization.
- Large amplitude, long-duration, polyphasic MUAPs are seen after 3–6 months as reinnervation occurs

SYMMETRIC, **PAINLESS**, DIABETIC POLYRADICULOPATHY OR RADICULOPLEXUS NEUROPATHY

Clinical Features

- Manifests as progressive, relatively painless, symmetrical proximal and distal weakness that typically evolves over weeks to months, such that it clinically resembles CIDP
- Whether this neuropathy represents the coincidental occurrence of CIDP in a patient with DM, or this is a distinct form of diabetic neuropathy, is unclear and controversial
- This type of neuropathy occurs in both type 1 and type 2 DM.
- **The pattern of weakness resembles CIDP in that there is symmetric distal and proximal weakness affecting the legs more than the arms.**
- Distal muscles are more affected than proximal muscles.

- Onset of weakness is not heralded or accompanied by such severe back and proximal leg pain, and the motor weakness is relatively symmetric.
- Distal dysesthesias, perhaps secondary to a superimposed DSPN, are occasionally present.

EDX

- NCS:
- Demonstrate mixed axonal and demyelinating features, with absent or reduced SNAP
- CMAP amplitudes combined with slowing of NCVs,
- prolongation of distal latencies, and absent or prolonged latencies of F waves.
- Rarely, conduction block and temporal dispersion are found.
- Occasionally, the electrophysiological features can fulfill research criteria for demyelination, but these patients generally have patterns that are more axonal in nature than seen in idiopathic CIDP.
- EMG:
- Reveals fibrillation potentials and positive sharp waves diffusely, including multiple levels of the paraspinal musculature.
- Autonomic studies:
- May demonstrate abnormalities in sudomotor, cardiovagal, and adrenergic functions.

DIABETIC MONONEUROPATHIES OR MULTIPLE MONONEUROPATHIES

- Most of the time patients have underlying DSPN.
- Are usually insidious in onset and presumably mechanical in nature due to entrapment or compressive mechanisms.
- Mononeuropathies that have an abrupt onset and a presumed ischemic mechanism (e.g., a diabetic third nerve palsy), are more likely to occur in individuals not yet identified as being diabetic.
- The most common neuropathies are:
- - median neuropathy at the wrist
- - ulnar neuropathy at the elbow
- **Others:**
- - peroneal neuropathy at the fibular head
- - sciatic
- - lateral femoral cutaneous
- - cranial neuropathies

DIABETIC MONONEUROPATHIES OR MULTIPLE MONONEUROPATHIES

- In regard to cranial mononeuropathies:
- - seventh nerve palsy is most common,
- - Followed by:
- third, sixth, and, less frequently, fourth nerve palsies.

- The multiple mononeuropathies, perhaps in combination with a radiculoplexus neuropathy, may give the appearance of a mononeuropathy multiplex pattern

ACUTE TREATMENT–INDUCED PAINFUL NEUROPATHY

Clinical Features

- Some patients suffer from **severe acute neuropathic pain**:
- - may occur in the setting of DNC
- - anorexia associated with severe weight loss
- - rarely, severe pain develops soon after starting intensive glycemic treatment with rapid control of the glycemia, so called treatment-induced neuropathy or **insulin neuritis**

Clinical Features

- **Treatment-induced neuropathy or insulin neuritis**
- Can occur in patients with type 1 or type 2 diabetes following treatment with insulin or oral hypoglycemic agents.
- The pain is usually in a length-dependent distribution but can be diffuse.
- Many patients, particularly those with type 1 DM, suffer from autonomic symptoms (orthostatic lightheadedness, nausea, vomiting, diarrhea, early satiety, and erectile dysfunction in men).
- Worsening retinopathy also parallels the course of the neuropathic pain.
- On examination, pain and temperature sensation are reduced, while most patients have hyperalgesia and allodynia.
- Muscle strength is not impaired

EDX

- NCS:
- May be normal or abnormal, similar to DSPN.
- Autonomic testing:
- Usually reveals abnormal heart rate response to deep breathing and abnormal Valsalva ratio with diminished variability in the heart rate as well as orthostatic hypotension.

HYPOGLYCEMIA/HYPERINSULINEMIA

Clinical Features

- Polyneuropathy has been associated with persistent hypoglycemia secondary to an islet cell tumor of the pancreas, hyperinsulinemia, or in early stages of treatment of DM.
- **The neuropathy is characterized by progressive numbness and paresthesias in the hands and feet.**
- Over time, distal motor weakness and atrophy may develop.
- Muscle stretch reflexes are generally reduced in a length-dependent fashion.
- With correction of the hypoglycemia, the sensory symptoms usually improve; however, muscle atrophy and weakness often remain to some extent.

EDX

- NCS:
- SNAPs that are reduced in amplitude or absent.
- The CMAP amplitudes are slightly decreased, while the conduction velocities are normal or only mildly reduced.
- EMG:
- May demonstrate fibrillation potentials, positive sharp waves, and reduced recruitment of large polyphasic MUAPs in the distal limb muscles.