

Primer of Chronic Inflammatory Demyelinating Polyradiculoneuropathy

General: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is so named because it is an immune-mediated inflammatory neuropathy primarily affecting myelin covering nerve roots and peripheral nerves. While there are many similarities with acute inflammatory demyelinating polyradiculoneuropathy (AIDP) or the Guillain Barré syndrome (GBS) they are different disorders and CIDP is not chronic AIDP/GBS.

Clinical features: CIDP generally progresses over several months (>2 months) before it is diagnosed. Occasionally it may progress very rapidly and may be diagnosed as AIDP, but when progression exceeds 2 months the initial diagnosis is changed to CIDP. Rarely patients will describe natural (untreated) exacerbations and remissions, but most exacerbations reflect treatment withdrawal.

CIDP usually involves both sensory and motor nerves, but occasionally only sensory nerves will be affected. Because both nerve roots and peripheral nerves are involved at the onset symptoms do not follow a length-dependent pattern and there will

be numbness of arms and legs and weakness of proximal and distal muscles. Sensory symptoms are numbness and also gait ataxia. Motor symptoms are difficulty rising from a chair and stumbling. The distribution is usually symmetric. Symptoms may be mild but usually progress to be disabling.

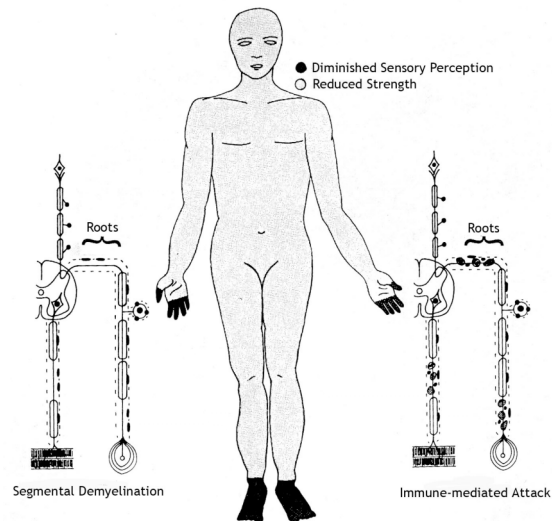


Figure: Diffuse weakness and distal sensory loss. Right: Immune-mediated attack affecting roots and nerves. Left: Resultant demyelination.

Genetics: CIDP is not a genetic disease.

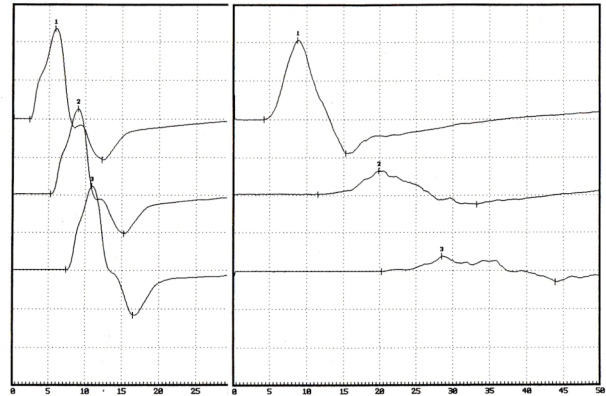
Diagnosis: CIDP is considered when symptoms progress more rapidly than typical length-

dependent neuropathies and the distribution of numbness and weakness includes arms and legs and both proximal and distal regions. Sensory symptoms are numbness and reduced sensory perception. Loss of proprioception (ability to sense body position in space) contributes to unsteadiness of gait. Motor symptoms are difficulty rising from a chair and climbing stairs and difficulty with gait, frequently leading to inability to walk.

Neurologic examination shows reduced perception of light touch to arms and legs and loss of ability to distinguish the vibration of a tuning fork applied to the finger of toe. There may be inability to detect, with eyes closed, up and down movements of the finger or toe. There will be weakness of proximal and distal muscles of arms and legs. Rising will be difficult and gait unsteady. Tendon reflexes are usually absent in the legs and absent or reduced in the arms.

Nerve conduction studies are important in demonstrating evidence of demyelination by showing slowed conduction and conduction block. Slowed conduction causes prolonged distal latencies, slowed conduction velocities, and

prolonged F-wave latencies. Conduction block affects the amplitude and shape of the waveform.



Left: Normal CMAP waveforms.
Right: Abnormal CMAP waveforms in CIDP showing prolonged distal latency, slowed responses and reduced and irregular waveforms due to demyelination and conduction block.

Because nerve roots are involved there is break down of the blood-nerve barrier and leakage of serum protein into spinal fluid increasing CSF protein levels. CSF cell count remains normal.

Pathogenesis: The pathophysiology is felt to be due to immune-mediated attack on myelin. The attack is mediated by both humeral and cellular components of the immune system. Trigger events are unknown, and unlike AIDP, antecedent illnesses (flu) are rare. The immune attack on myelin causes Schwann cell nuclei

to divide, and with remyelination the additional nuclei lead to shorter segments of myelin and some degree of permanent slowing of nerve conduction. The immune response may progress to include damage to axons and thus secondary denervation. Remyelination can occur rapidly (months) but axonal regeneration can be very slow (1 or more years) and incomplete, and residual weakness and numbness is attributed to axonal loss. Although no specific antibodies have been identified, a rapid component of improvement with treatment (days to weeks) is attributed to reduction of antibodies that functionally block nerve conduction.

Treatment: There are a number of available treatment options that have been demonstrated effective in randomized control trials and are generally felt to be therapeutically equal. Corticosteroids and Intravenous immune globulin (IVIG) directly affect (dampen) the immune system while plasma apheresis (plasma exchange) transiently reduces circulating humoral factors of the immune system. Prednisone is usually given 60 mg QD for 1 month and is followed by a very slow taper. IVIG is usually given 2 gm/kg (over 3-5 days) as the initial dose followed

by 1 gm/kg monthly for several months and followed by a slow taper. Plasma exchange is a process of removing a portion of whole blood, separating and discarding the plasma portion and returning the red and white cell portion. Three to four cycles are carried out to remove a suitable amount of plasma. The therapeutic rationale is removal of the humoral component of the immune response, and thus is usually combined with prednisone to dampen the immune system.

Medications for numbness are drugs used for neuropathic pain in other neuropathies and include gabapentin (Neurontin®) and pregabalin (Lyrica®) and antidepressants that include amitriptyline (Elavil®), imipramine (®) and duloxetine (Cymbalta®).

Management: Treatment regimens vary among patients and may require trial-and-error to determine the most effective drug and taper schedule. Occasional patients will respond to prednisone or IVIG, but most respond to either, and the choice depends upon past medical history (prednisone complicates glucose control in the setting of diabetes) and financial issues (IGIV is expensive). Few patients do well with no medication and

determining a maintenance dose can be challenging.

The ultimate response to treatment varies among patients in part due to the degree of axonal damage. Most patients regain a large degree of function, but may not ambulate easily. Many have a residual degree of numbness.

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