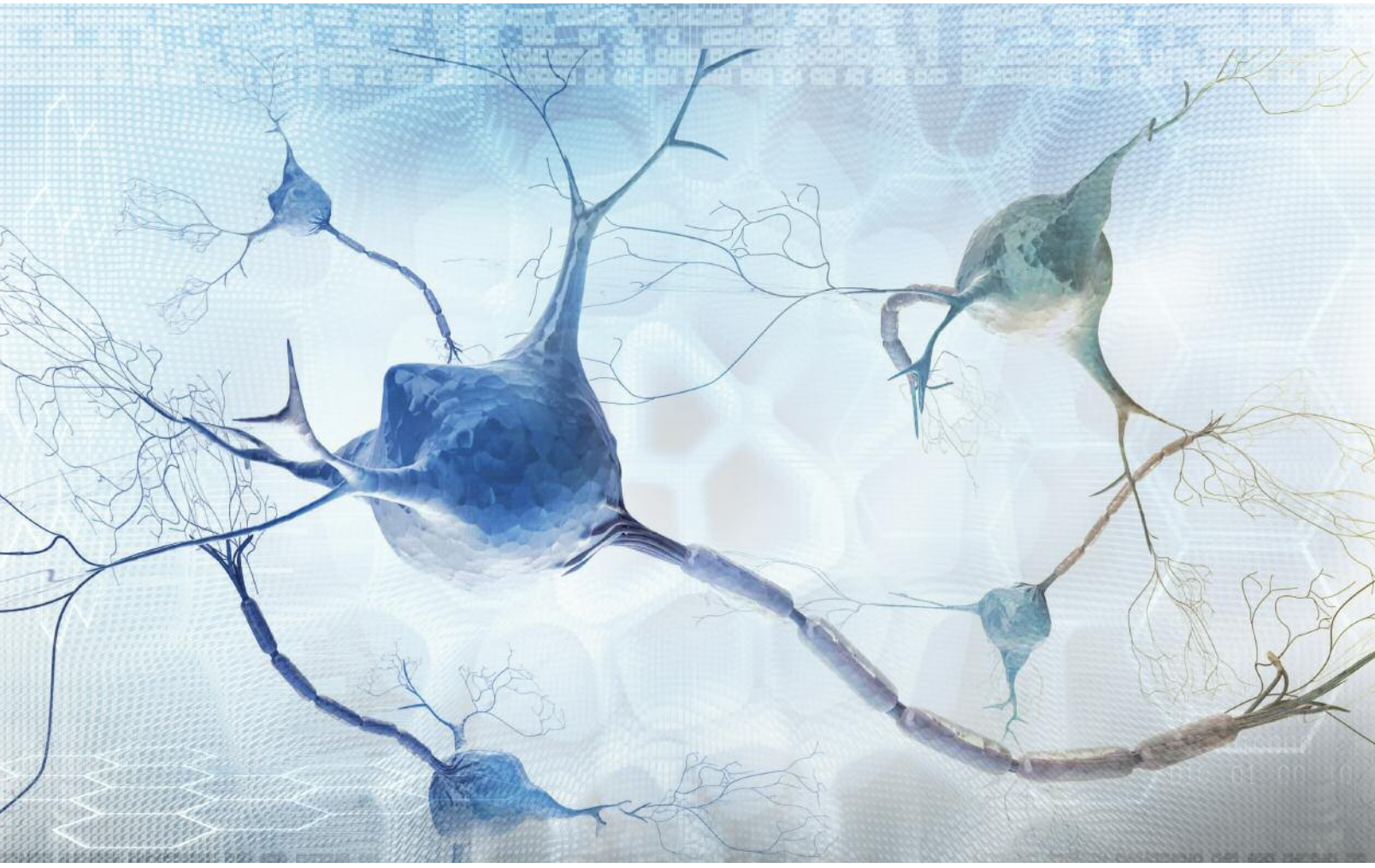
Diagnosing and Treating Chronic Inflammatory Demyelinating Polyneuropathy



This autoimmune disease is difficult to diagnose due to its rarity and many variants, but once it is diagnosed, there are treatment options.

By Michelle Greer, RN, and Gil I. Wolfe, MD, FAAN

The primary function of the immune system is to differentiate between self and non-self, to keep self healthy and to destroy or neutralize non-self. When the immune system malfunctions and attacks itself, it is known as an autoimmune disease. Chronic inflammatory demyelinating polyneuropathy (CIDP) is considered an autoimmune disease. CIDP occurs when the myelin sheath that covers the nerves and assists with impulse transmission is attacked. This is known as demyelination. Due to the nature of the immune attack, there is usually inflammation. The result is an interruption in nerve signals between the peripheral nerves and the muscles they control.

CIDP presents slowly, usually over several months, unlike the acute form of demyelinating neuropathy, which is known as Guillain-Barré syndrome (GBS). GBS presents rapidly, usually over days, but sometimes even more quickly, and frequently, it occurs following some sort of infection or illness. Unlike GBS, CIDP is usually a chronically progressive neuropathy, and it is rarely associated with antecedent illnesses or respiratory failure.[1]

Diagnosing CIDP

Usually, CIDP presents as a motor predominant neuropathy with prominent proximal weakness, meaning the muscles responsible for movement closest to the torso are affected first. The weakness is typically symmetrical, affecting both sides of the body equally. Occasionally, CIDP can present in the pattern of a mononeuropathy multiplex, large-fiber neuropathy with sensory ataxia, pure motor neuropathy or small-fiber neuropathy.[1]

It's not uncommon for CIDP to go undiagnosed for a while due to many factors. The symptoms may be vague and brushed off until they become more profound and/or interfere with everyday functioning. And once an individual does go to a physician, a definitive diagnosis still may not follow.

Neuropathy has many causes, and CIDP has several variants (see Table 1).[2] Therefore, it is important that a

Table 1. CIDP and Variants

A. Symmetric proximal and distal motor predominant CIDP
B. Lewis-Sumner syndrome (LSS) (or multifocal acquired demyelinating sensory and motor neuropathy)
C. Demyelinating neuropathy with IgG or IgA paraprotein
D. Sensory predominant demyelinating neuropathy
E. CIDP neuropathy with central nervous system (CNS) demyelination
F. Demyelinating neuropathy associated with systemic disorders:
   1. Hepatitis B or C
   2. HIV
   3. Lymphoma
   4. Diabetes mellitus
   5. Systemic lupus erythematosus or other collagen vascular disorders
   6. Thyrotoxicosis
   7. Organ or bone marrow transplants
   8. Nephrotic syndrome
   9. Inflammatory bowel disease
G. CIDP in patients who have inherited neuropathy

Source: Lewis, RA. Chronic Inflammatory Demyelinating Polyneuropathy, *Neurologic Clinics*, 25 (2007) 71–87.

Table 2. Diagnostic Tests

Test	What is it?
Electromyography (EMG)*	A procedure to measure and record muscle activity to show which muscles and nerves are affected.
Nerve Conduction Study (NCS)*	A procedure to measure the speed and efficiency of electrical signals of the nerves.
Lumbar Puncture	A spinal tap to look at the cerebral spinal fluid for abnormalities. Protein in the CSF is usually indicative of an immune response and can be present in CIDP.
Nerve Biopsy	A section of the nerve is taken and examined to look for cause of damage. Only done if diagnosis is unclear.

*An EMG and NCS are almost always both conducted in order to appropriately diagnose CIDP.

thorough health history and physical and neurological examination be performed to determine the cause of the neuropathy. CIDP is rare, but its incidence ranges greatly due to the potential of over- or underdiagnosis. An individual may be thought to have CIDP when it is actually another form of neuropathy, and the reverse can happen as well. Many physicians and patient groups have worked on a standard way to identify CIDP more quickly and accurately, but appropriate diagnosis remains a challenge.

Symptoms are first noticed as numbness, tingling, pain and weakness, which are vague and can be the initial symptoms of many conditions. This usually occurs first in the toes and feet, eventually resulting in foot drop or drag and increased difficulty in walking. The weakness and numbness are typically symmetrical — equal on both sides of the body — and sensory loss is often in a stocking and glove distribution.

A diagnosis of CIDP is based on an electrophysiologic pattern of multifocal demyelination identified through an EMG/nerve conduction study, elevated CSF (cerebral spinal

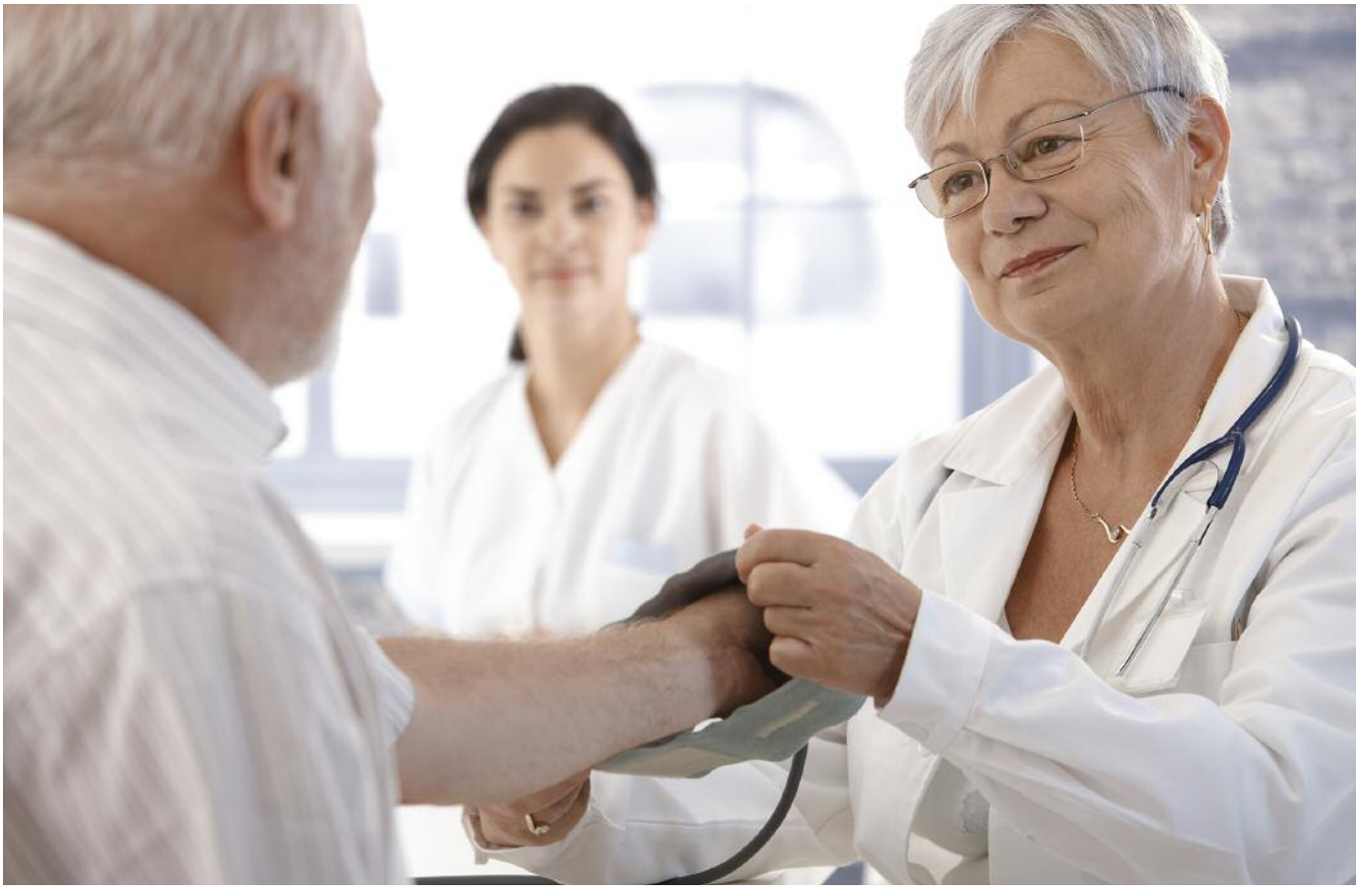
Table 3. Standard Immunotherapy for Immune-Mediated Neuropathies

Therapy	Neuropathy Types	Route	Starting Doses	Maintenance Doses
Prednisone*	CIDP, VN	Oral	60-100 mg/day for 4 weeks	60-100 mg every other day, reducing dose by 10 mg every 2-4 weeks. In diabetics, consider daily dosing to simplify glucose control
Methylprednisolone*	CIDP, VN	IV	1 gram daily or every other day for a total of 3-5 doses	Reduce dose by 10 mg
Azathioprine (Imuran)*	CIDP	Oral	50 mg/day	Increase by 50-mg increments every 2-4 weeks to 2-3 mg/kg/day
Cyclophosphamide (Cytoxan)*	CIDP, VN, MMN	Oral	50 mg/day	Increase to 1.5-2 mg/kg/day
Cyclophosphamide	CIDP, VN, MMN	IV	0.5-3 gm/m2	Repeat dose monthly for 6 months
Cyclosporine (Neoral, Sandimmune)*	CIDP	Oral	100 mg twice daily	Increase by 100-mg increments to 3-6 mg/kg/day on a twice daily schedule
IVIG	GBS*, CIDP, MMN	IV	2 gm/kg divided over 2-5 days	0.4-1 gm/kg as a single dose every 3-8 weeks as needed
Plasmapheresis	GBS, CIDP, MMN	IV	Exchange total of 250 mL/kg plasma	Total exchanges of 50-250 mL/kg may be repeated as needed over 7-14 days
Rituximab (Rituxan)*	MMN, IgM-associated neuropathy	IV	375 mg/m2 every week x 4 weeks	Repeat 375 mg/m2 as needed 9-15 months later

Abbreviations: CIDP=chronic inflammatory demyelinating polyneuropathy; GBS=Guillain-Barré syndrome; IgM=immunoglobulin M; IVIG=intravenous immunoglobulin; MMN=multifocal motor neuropathy; VN=vasculitic neuropathy.

* Not FDA approved for this indication.

Source: Trivedi, JR, and Wolfe, GI. Peripheral Neuropathies. In: Rakel, RE, and Bope, ET (eds.) *Conn's Current Therapy*. Philadelphia: W.B. Saunders, 2005; pp 1086-1096.



fluid) protein and, when necessary, nerve biopsy. These tests, combined with a thorough health history and neurological exam, will help guide the physician to a correct diagnosis (see Table 2).

Treating CIDP

Once CIDP is diagnosed, treatment options are considered and discussed. The treatment of CIDP is based on immunomodulating therapies that are summarized in Table 3. Immunomodulation refers to suppression or alteration of the immune response so that attack on the self subsides and symptoms improve. CIDP does respond to corticosteroids; however, long-term use of high-dose steroids comes with its own set of issues. Side effects can be severe and affect multiple organ systems. Plasmapheresis is generally reserved for refractory patients — those who have tried all the standard therapies and the condition is still not controlled.[2] The only treatment that has received U.S. Food and Drug Administration (FDA) approval for the management of CIDP is intravenous immunoglobulin (IVIG).

Rare, but There Is Hope

Although CIDP is rare and difficult to diagnose, once it is accurately diagnosed, there are treatment options. CIDP can be treated with a variety of immunomodulatory therapies, including FDA-approved IVIG. Fortunately, CIDP can be managed to help patients live relatively normal and healthy lives, and there are many patient-to-patient support groups that include oversight by experts in neuromuscular disorders. ■

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References

1. Trivedi, JR, and Wolfe, GI. Peripheral Neuropathies. In: Rakel, RE, and Bope, ET (eds.) *Conn's Current Therapy*. Philadelphia: W.B. Saunders, 2005; pp 1086-1096.
2. Lewis, RA. Chronic Inflammatory Demyelinating Polyneuropathy, *Neurologic Clinics*, 25 (2007) 71–87.