

## THERAPIES IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)

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Chronic inflammatory demyelinating polyneuropathy (CIDP) is the most common chronic, acquired immune-mediated disease of the peripheral nervous system with a prevalence of up to 9/100,000. Because it is a treatable form of chronic polyneuropathy, prompt recognition is needed to improve outcome. In CIDP, motor and sensory signs develop slowly, over months, with a minimum of 2 months from the outset. Patients with typical CIDP present with symmetrical proximal and distal weakness, diminished or absent tendon reflexes, symmetrical distal sensory deficits, elevation of the spinal fluid (CSF) protein, demyelination with conduction block on electrophysiology and histological signs of demyelination. Disease variants characterized by asymmetry, prominent motor or sensory deficits and multifocal symptoms are increasingly recognized and may generate diagnostic challenges. About 10-15% of CIDP patients may present acutely resembling Guillain Barré syndrome (GBS) and require early recognition because therapeutic strategies in this subset may be different from the outset.

Both cellular and humoral factors have been implicated in the immunopathogenesis of CIDP. T cells, activated macrophages, cytokines, costimulatory molecules and antibodies operate in concert with each other. The increasingly recognized concomitant axonal loss secondary to primary demyelination remains an important factor in therapeutic approaches. Up to 10% of CIDP patients have IgG4 antibodies to paranodal proteins, *neurofascin-155 and contacting/Caspr 1 (CNTN1)*, and may represent a distinct subset relevant to therapies because many of them are suboptimally responding to IVIg.

Control trials have demonstrated the efficacy of IVIg, plasmapheresis and corticosteroids in most patients. Results and lessons learnt from the largest ever conducted study with IVIg (the ICE trial) after which IVIg gained FDA-approval, suggest that early treatment with IVIg is effective, well tolerated and prevents axonal degeneration; it is therefore preferable to corticosteroids or plasmapheresis. Controlled trials with beta-interferon and Methotrexate have failed; the other immunosuppressants such as Cyclosporin, Mycophenolate, Rituximab, or Cyclophosphamide may

occasionally offer some benefit but controlled studies have not been performed. At least 15% of CIDP patients initially responding to IVIg, continue receiving it for long periods and seem to be “over-treated” because their disease has been in remission or burnt-out; periodic checks to assess whether further treatment with IVIg is needed is therefore essential . Up to 30% of CIDP patients do not adequately respond to available therapies, and new therapeutic strategies are explored in ongoing clinical trials.