PRACTICAL POINTS IN CIDP MANAGEMENT

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CONTENT

The heterogeneity of CIDP

Clinicopathological correlation

Diagnostic flow

Treatment options
- IVIg
- Steroid
- Other immunosuppressive agents

Guideline

CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)

- Most common treatable chronic neuropathy worldwide
- Prevalence ranging from ~1 to 9 cases per 100,000
- CIDP spectrum: relatively heterogeneous

- Many sets of diagnostic criteria : based largely on electrophysiological findings

CIDP KEY FEATURES

Progression over at least two months

Weakness more than sensory symptoms

Symmetric involvement of arms and legs

Proximal muscles involved along with distal muscles

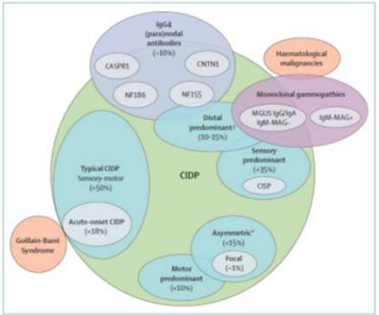
Reduced deep tendon reflexes throughout

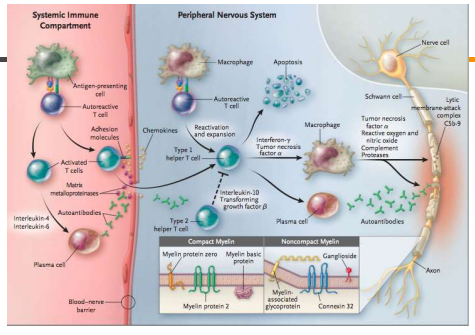
Increased cerebrospinal fluid protein without pleocytosis

Nerve conduction evidence of a demyelinating neuropathy

Nerve biopsy evidence of segmental demyelination with or without inflammation

THE HETEROGENEITY OF CIDP





Neuromuscular
RESEARCH PAPER

Clinicopathological characteristics of subtypes of chronic inflammatory demyelinating polyradiculoneuropathy

Shohei Ikeda,[1] Haruki Koike,[1,2] Ryoji Nishi,[1] Yuichi Kawagashira,[1] Masahiro Iijima,[1] Masahisa Katsuno,[1] Gen Sobue[1,3]

Conclusions

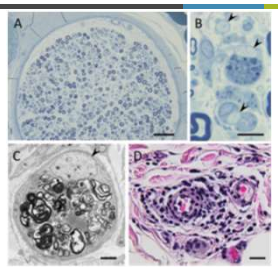
Preferential involvement of distal and proximal segments and uniform pathological features in typical CIDP indicate a role of humoral factors at site where the blood–nerve barrier is deficient.

By contrast, focal lesions in MADSAM, DADS and pure sensory forms may share neuropathic mechanisms primarily affecting the nerve trunk.

Ikeda S, *et al*. *J Neurol Neurosurg Psychiatry* 2019;**0**:1–8. doi:10.1136/jnnp-2019-320741

SURAL NERVE BIOPSY IN TYPICAL CIDP

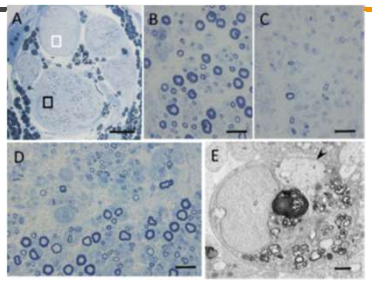
A: Preserved fiber, little onion bulbs, few axonal sprouts
B. Naked axon
C. EM: degradation of myelin by macrophage
D. Small lymphocytes infiltration at epineurium



Ikeda S, *et al*. *J Neurol Neurosurg Psychiatry* 2019;**0**:1–8. doi:10.1136/jnnp-2019-320741

MADSAM

A. Variation of myelinated nerve fiber density (focal reduction)
B. Preserved myelinated fiber
C. Loss of large myelinated fibers, compared with small fiber
D. Intrafascicular variation and among fascicles
E. Macrophage-induced demyelination (similar to typical CIDP)



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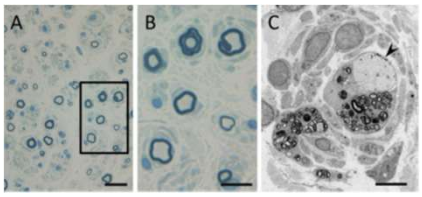
DISTAL ACQUIRED DEMYELINATING SYMMETRIC GROUP (DADS)

A. Conspicuous onion bulbs, extreme variation in myelinated fiber density
B. High power of A
C. Macrophage – induced demyelination

Arrow: naked axon



Ikeda S, *et al*. *J Neurol Neurosurg Psychiatry* 2019;**0**:1–8. doi:10.1136/jnnp-2019-320741

Table 2 | Characteristic abnormalities found in different diagnostic tests

Neuropathy	Electrodiagnostic tests	Serological tests	Nerve biopsy
Chronic inflammatory demyelinating polyneuropathy (CIDP)	Multifocal demyelinating abnormalities	None	Segmental demyelination and remyelination Loss of large myelinated axons 'Onion bulbs'
Anti-MAG neuropathy	Disproportionate prolongation of distal latencies	IgM monoclonal gammopathy Elevated titres of anti-MAG/SGPG antibodies	Demyelination with loss of large myelinated axons Separation of the myelin lamellae at the minor dense line Deposits of IgM and C3d on myelin sheaths
Multifocal motor neuropathy	Multifocal motor conduction block	Elevated anti-GM1 ganglioside antibodies (50% of cases)	Axonal degeneration Regenerative axonal clusters in motor nerves
POEMS syndrome	Uniform demyelinating changes	λ light chain IgG or IgA monoclonal gammopathy Elevated vascular endothelial growth factor levels	Demyelination with loss of large myelinated axons Separation of the myelin lamellae at the major dense line

Abbreviations: MAG, myelin-associated glycoprotein; SGPG, sulphated glucuronyl paragloboside.

Latov, N. Nat. Rev. Neurol. 10, 435–446 (2014)

TYPICAL CIDP

	Epidemiology	Clinical symptoms	Distribution of symptoms	Treatment response	Mimics and additional information
Typical CIDP					
Sensory-motor[4,6,7]	>50%	Chronic onset; motor and sensory	Symmetric; usually proximal rather than distal	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective	Other more common sensory-motor neuropathies (eg, paraproteinemic or hereditary neuropathy)
Acute onset[4,6,8]	Around 18%	Subacute onset; motor and sensory	Symmetric; proximal and distal	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective	Guillain-Barré Syndrome; might resemble patients with NF155 and CNTN1 antibodies

ATYPICAL CIDP VARIANTS

Atypical CIDP variants				
Asymmetric[4,5,7]	8-15%	Chronic onset; motor and sensory	Asymmetric; distal rather than proximal; upper rather than lower limbs	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective
Focal[3,5,7]	Around 1%	Chronic onset; slow disease progression; motor and sensory	Brachial or lumbosacral plexus or one or more peripheral nerves in one limb; proximal and distal; upper and lower limbs	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective
Distal predominant[3,5,7]	2-10%	Chronic onset; sensory more than motor	Symmetric; distal rather than proximal	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective (if MAG antibodies not present)
Motor predominant[4,7]	4-10%	Chronic onset; motor more than sensory	Symmetric; proximal and distal	Intravenous immunoglobulins effective; patients' condition might deteriorate after corticosteroids
Sensory predominant[4,5,7,8] (including CISP)	4-35%	Chronic onset; sensory more than motor; sensory ataxia (in CISP)	Symmetric; distal rather than proximal; upper rather than lower limbs	Intravenous immunoglobulins, corticosteroids, and plasma exchange effective

Lancet Neurol 2015; Published Online May 7, 2015

IGG4 AB AGAINST NODAL-PARANODAL PROT

Phenotype with IgG4 antibodies against nodal and paranodal proteins				
NF155[2,10,15,16,17,18,19,20,21,22]	4-18%	Subacute severe onset at around age 25 years; motor more than sensory; sensory ataxia; tremor	Symmetric; distal rather than proximal	Poor response to intravenous immunoglobulins; partial response to corticosteroids; potentially good response to rituximab and plasma exchange
NF140 and NF186[2,18]	2-5%	Subacute onset; motor and sensory; sensory ataxia; cranial nerve deficits can occur	Symmetric	Partial response to intravenous immunoglobulins and corticosteroids; potentially good response to rituximab
CNTN1[15,16,17,18,19,20]	1-7%	Subacute severe onset at around age 25 years; motor more than sensory; sensory ataxia; tremor	Symmetric; proximal and distal	Poor response to intravenous immunoglobulins; partial response to corticosteroids; potentially good response to rituximab
CASPR1[16,20]	1-3%	Subacute severe onset; motor more than sensory; neuropathic pain	Symmetric; distal rather than proximal	Poor response to intravenous immunoglobulins; potentially good response to rituximab

Lancet Neurol 2015; Published Online May 7, 2015

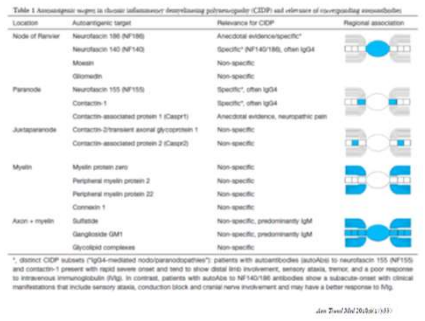


Table 1 Autoantigenic targets in chronic inflammatory demyelinating polyneuropathy (CIDP) and relevance of corresponding autoantibodies

Location	Autoantigenic target	Relevance for CIDP	Regional association
Node of Ranvier	Neurofascin 186 (NF186)	Anecdotal evidence/specific*	
	Neurofascin 140 (NF140)	Specific* (NF140/186), often IgG4	
	Moesin	Non-specific	
	Gliomedin	Non-specific	
Paranode	Neurofascin 155 (NF155)	Specific*, often IgG4	
	Contactin-1	Specific*, often IgG4	
	Contactin-associated protein 1 (Caspr1)	Anecdotal evidence, neuropathic pain	
Juxtaparanode	Contactin-2/transient axonal glycoprotein 1	Non-specific	
	Contactin-associated protein 2 (Caspr2)	Non-specific	
Myelin	Myelin protein zero	Non-specific	
	Peripheral myelin protein 2	Non-specific	
	Peripheral myelin protein 22	Non-specific	
	Connexin 1	Non-specific	
Axon + myelin	Sulfatide	Non-specific, predominantly IgM	
	Ganglioside GM1	Non-specific, predominantly IgM	
	Glycolipid complexes	Non-specific	

*, distinct CIDP subsets ("IgG4-mediated nodo/paranodopathies"): patients with autoantibodies (autoAbs) to neurofascin 155 (NF155) and contactin-1 present with rapid severe onset and tend to show distal limb involvement, sensory ataxia, tremor, and a poor response to intravenous immunoglobulin (IVIg). In contrast, patients with autoAbs to NF140/186 antibodies show a subacute-onset with clinical manifestations that include sensory ataxia, conduction block and cranial nerve involvement and may have a better response to IVIg.

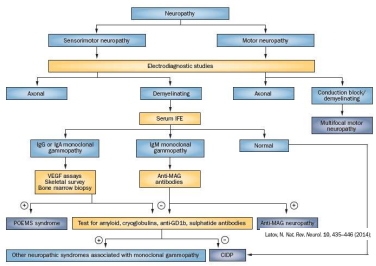
Ann Transl Med 2016;4(14):333

EFNS CIDP CRITERIA

Table 4 Clinical diagnostic criteria

(1) Inclusion criteria
  (a) Typical CIDP
    Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months; cranial nerves may be affected; and
    Absent or reduced tendon reflexes in all extremities
  (b) Atypical CIDP (still considered CIDP but with different features)
    One of the following, but otherwise as in (a) (tendon reflexes may be normal in unaffected limbs):
    Predominantly distal (distal acquired demyelinating symmetric, DADS) or
    Asymmetric [multifocal acquired demyelinating sensory and motor neuropathy (MADSAM), Lewis-Sumner syndrome] or
    Focal (e.g., involvement of the brachial or lumbosacral plexus or of one or more peripheral nerves in one upper or lower limb)
    Pure motor or
    Pure sensory (including chronic immune sensory polyradiculopathy affecting the central process of the primary sensory neuron)
(2) Exclusion criteria
  Borrelia burgdorferi infection (Lyme disease), diphtheria, drug or toxin exposure probably to have caused the neuropathy
  Hereditary demyelinating neuropathy
  Prominent sphincter disturbance
  Diagnosis of multifocal motor neuropathy
  IgM monoclonal gammopathy with high titre antibodies to myelin-associated glycoprotein
  Other causes for a demyelinating neuropathy including POEMS syndrome, osteosclerotic myeloma, diabetic and non-diabetic lumbosacral radiculoplexus neuropathy. PNS lymphoma and amyloidosis may occasionally have demyelinating features

DIAGNOSTIC PATHWAY



Latov, N. Nat. Rev. Neurol. 10, 435–446 (2014)

INVITED REVIEW

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND MALIGNANCY: A SYSTEMATIC REVIEW

YUSUF A. RAJABALLY, MD, FRCP[1,2] and SHAHRAM ATTARIAN, MD, PhD[3,4]

Muscle Nerve. 2018 Jun;57(6):875-883.

CIDP frequently precedes the malignancy diagnosis

Most common : Hematological disorders, particulary non- Hodgkin lymphoma.

Second most common: Melanoma, may be accompanied by antiganglioside Ab

Other cancers are rare, with variable timings and presentations but good responses to immunomodulation and/or cancer therapy.

Unusual neurological features such as ataxia, distal/upper limb predominance, or cranial/respiratory/autonomic involvement may suggest associated malignancy as may abdominal pain, diarrhea/constipation, poor appetite/weight loss, dermatological lesions, and lymphadenopathy

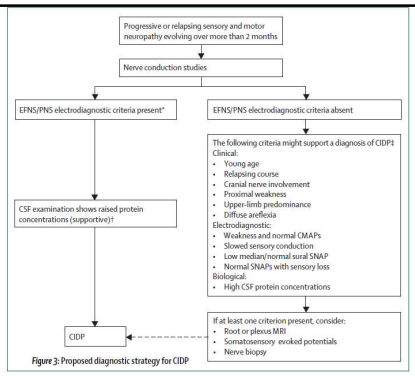


Figure 3: Proposed diagnostic strategy for CIDP

Table 1 Electrodiagnostic criteria

(1) Definite: at least one of the following
(a) Motor distal latency prolongation ≥30% above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), or
(b) Reduction of motor conduction velocity ≥30% below LLN in two nerves, or
(c) Prolongation of F-wave latency ≥30% above ULN in two nerves (≥50% if amplitude of distal negative peak CMAP <80% of LLN values), or
(d) Absence of F-waves in two nerves if these nerves have distal negative peak CMAP amplitudes ≥20% of LLN + ≥1 other demyelinating parameter[a] in ≥1 other nerve, or
(e) Partial motor conduction block: ≥50% amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP ≥ 20% of LLN, in two nerves, or in one nerve + ≥1 other demyelinating parameter[a] in ≥1 other nerve, or
(f) Abnormal temporal dispersion (>30% duration increase between the proximal and distal negative peak CMAP) in ≥2 nerves, or
(g) Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥1 nerve (median ≥ 6.6 ms, ulnar ≥ 6.7 ms, peroneal ≥ 7.6 ms, tibial ≥ 8.8 ms)[b] + ≥1 other demyelinating parameter[a] in ≥1 other nerve
(2) Probable
≥30% amplitude reduction of the proximal negative peak CMAP relative to distal, excluding the posterior tibial nerve, if distal negative peak CMAP ≥ 20% of LLN, in two nerves, or in one nerve + ≥1 other demyelinating parameter[a] in ≥1 other nerve
(3) Possible
As in (1) but in only one nerve

Neuromuscular
RESEARCH PAPER

Atypical CIDP: diagnostic criteria, progression and treatment response. Data from the Italian CIDP Database

Box 1 Proposed clinical diagnostic criteria for atypical CIDP

DADS
Mandatory criteria
(A) with or (B) without increased distal motor latency
1. Symmetric, sensory or sensorimotor symptoms and signs starting distally in the lower limbs, without proximal limb–trunk–face involvement (length-dependent fashion).*
Other possible symptoms
1. Ataxia, neuropathic pain, cramps, fatigue, autonomic symptoms, tremor.
2. Upper-limb distal sensory or sensorimotor symptoms and signs occurring later (at least after 1 year from onset).
Exclusion criteria
1. Cranial nerve involvement.
2. Proximal limbs, trunk, face involvement.
3. Weakness without sensory symptoms.
4. Symptoms and signs starting in the upper limbs.

PURE SENSORY CIDP
Mandatory criteria
(A) with or (B) without abnormal motor nerve conduction studies
1. Sensory symptoms (including ataxia), without weakness, in a polyneuropathic distribution, symmetric or asymmetric.*
2. Symptoms may start anywhere in the body excluding a length-dependent pattern (included under DADS).
Other possible symptoms
1. Neuropathic pain, fatigue, tremor.
2. Facial sensory symptoms.
Exclusion criteria
1. Motor symptoms/signs including cramps and motor cranial nerve palsy.
2. Multifocal distribution.
3. Autonomic dysfunction.

CISP
Mandatory criteria
1. Sensory symptoms with a polyneuropathic distribution without weakness.*
2. Normal motor and sensory nerve conduction and EMG studies.
PLUS at least two of the following:
2. Abnormal SSEP not due to CNS involvement.
3. MRI showing gadolinium enhancement and/or hypertrophy of the cauda equina, lumbosacral or cervical nerve roots, or the brachial or lumbosacral plexuses.
4. Elevated CSF protein level with normal cells.
Exclusion criteria and other possible symptoms
1. As in pure sensory CIDP.

PURE MOTOR CIDP
Mandatory criteria
(A) with or (B) without abnormal sensory nerve conduction studies
1. Weakness, without sensory symptoms or signs, in a polyneuropathic distribution, symmetric or asymmetric.*
2. Symptoms may start anywhere in the body.
Other possible symptoms
1. Cramps, fatigue, tremor.
2. Motor cranial nerve palsy.
Exclusion criteria
1. Sensory symptoms/signs including sensory ataxia.
2. Autonomic dysfunction.
3. Neuropathic pain.
4. Multifocal distribution.

LSS
Mandatory criteria
(A) with or (B) without motor conduction block
1. Sensory symptoms, with or without weakness, in a multifocal distribution (unilateral focal† CIDP included).*
2. Symptoms may start anywhere in the body.
Other possible symptoms
1. Cramps, fatigue, autonomic symptoms, ataxia, neuropathic pain.
2. Motor and/or sensory cranial nerve palsy.
Exclusion criteria
1. Weakness in isolation, without sensory symptoms.
2. Symptoms/signs in a polyneuropathic distribution.

*Clinical phenotype must have lasted at least 1 year (temporal criterion).
†Focal CIDP defined as the presence of symptoms homogeneously restricted to the nerves of one limb or two limbs (ipsilateral upper and lower limb).
CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CISP, chronic immune sensory polyradiculopathy; CNS, central nervous system; CSF, cerebrospinal fluid; DADS, distal acquired demyelinating symmetric neuropathy; EMG, electromyography; LSS, Lewis-Sumner syndrome; SSEP, somatosensory evoked potential.

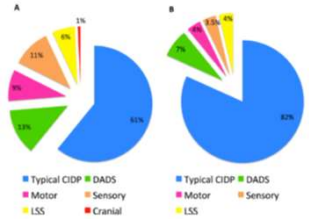


Figure 1 (A) CIDP type at 1 year after onset of symptoms; (B) CIDP type at study entry (mean 8 years after onset). Graphs show the frequency of the atypical CIDP variants at 1 year after the onset of symptoms (A) and at study entry (B) in 460 patients. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DADS, distal acquired demyelinating symmetric neuropathy; LSS, Lewis-Sumner syndrome.

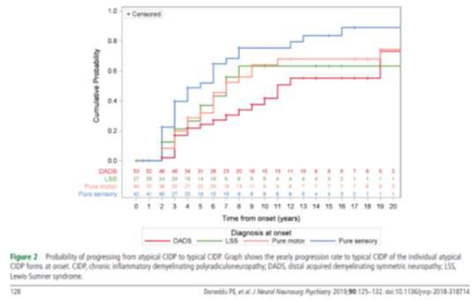


Figure 2 Probability of progressing from atypical CIDP to typical CIDP. Graph shows the yearly progression rate to typical CIDP of the individual atypical CIDP forms at onset. CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DADS, distal acquired demyelinating symmetric neuropathy; LSS, Lewis-Sumner syndrome.

Table 1 Comparison of clinical features and treatment response in atypical and typical CIDP

	DADS (n=34)	Pure sensory (n=16)	Pure motor (n=17)	LSS (n=17)	Typical CIDP (n=376)	P values
Gender (M:F)	24:10	10:6	8:9	16:1	235:141	0.0079*
Age at onset, years; mean (range)	58 (20–79)	57 (31–75)	53 (11–82)	48 (27–75)	49 (5–86)	0.0032†
Disease duration, years; mean (range)	8 (0.5–26)	5 (0.5–17)	10 (0.5–28)	7 (0.5–24)	8.5 (0.5–60)	NS
Fulfilment of EFNS/PNS criteria	24 (70.5%)	12 (75%)	15 (88%)	13 (76%)	310 (82%)	NS
Increased CSF proteins; positive/tested	26/29 (90%)	10/15 (67%)	7/9 (78%)	5/13 (38%)	243/284 (85.5%)	0.0002*
Mean CSF proteins, mg/dL (range)	93 (52–379)	86 (46–193)	171 (47–679)	82 (61–146)	123 (46–1000)	NS
Nerve imaging; positive/tested	7/7	5/5	0/0	6/7 (86%)	26/36 (72%)	NS
Nerve biopsy; positive/tested	2/4 (50%)	1/4 (25%)	0/0	0/1	21/36 (58%)	NS
MRC sum score; mean (range)	58 (48–60)	60 (60–60)	51 (36–60)	57 (49–60)	53.5 (26–60)	0.0003†
I-RODS score; mean (range)	39 (16–48)	38 (23–47)	31 (11–48)	40 (26–47)	33 (1–48)	0.0027†; 0.0301*
INCAT disability score; mean (range)	1.5 (0–6)	1.7 (0–3)	3.5 (0–10)	2 (0–6)	2.7 (0–10)	0.0005†
Quality of life score; mean (range)	7 (1–9)	7 (5–9)	8 (5–13)	7 (5–9)	8 (5–14)	0.0030†
Overall treatment response	16/25 (64%)	9/10 (90%)	15/17 (88%)	10/15 (67%)	299/344 (87%)	0.0050†; 0.0433*
EFNS/PNS only‡	9/15 (60%)	8/8 (100%)	14/15 (93%)	7/11 (64%)	191/216 (88%)	0.0107†; 0.0075*
Corticosteroids	9/16 (56%)	4/6 (67%)	3/7 (43%)	6/9 (67%)	110/215 (51%)	NS
Intravenous immunoglobulin	9/18 (50%)	6/7 (86%)	14/17 (82%)	5/12 (42%)	233/299 (78%)	0.0178†; 0.0086*
EFNS/PNS only‡	6/12 (50%)	4/5 (80%)	13/16 (82%)	3/9 (33%)	139/185 (75%)	0.0852†; 0.0123*

CIDP varies during the disease course. DADS and LSS have a less frequent response to intravenous immunoglobulin compared with typical CIDP, raising the possibility of a different underlying pathogenetic mechanism.

INVESTIGATIONS

Table 2 Investigations to be considered

To diagnose chronic inflammatory demyelinating polyradiculoneuropathy
- Electrodiagnostic studies including sensory and motor nerve conduction studies, which may be repeated, performed bilaterally, or use proximal stimulation for motor nerves
- CSF examination including cells and protein
- MRI spinal roots, brachial plexus, and lumbosacral plexus
- Nerve biopsy

To detect concomitant diseases
(a) Recommended studies
- [a]Serum and urine paraprotein detection by immunofixation
- Fasting blood glucose
- Complete blood count
- Renal function
- Liver function
- Antinuclear factor
- Thyroid function

(b) Studies to be performed if clinically indicated
- [a]Skeletal survey
- Oral glucose tolerance test
- Borrelia burgdorferi serology
- C reactive protein
- Extractable nuclear antigen antibodies
- Chest radiograph
- Angiotensin-converting enzyme
- HIV antibody

To detect hereditary neuropathy
- Examination of parents and siblings
- Appropriate gene testing (especially PMP22 duplication and connexin 32 mutations)
- Nerve biopsy

[a]Repeating these should be considered in patients who are or become unresponsive to treatment.

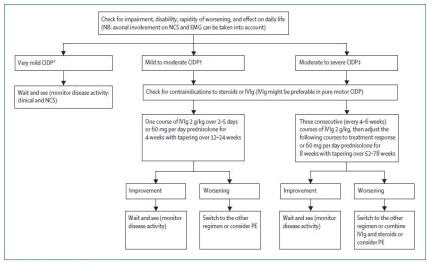


Figure 4 Proposed algorithm for CIDP treatment
At any step, if treatment fails, consider the following diagnoses: POEMS syndrome, lymphoma, amyloidosis, or sarcoidosis. If the patient still worsens under treatment or needs constant treatment maintenance, consider adding an immunosuppressant. CIDP=chronic inflammatory demyelinating polyradiculoneuropathy. EMG=electromyography. IVIg=intravenous immunoglobulin. NCS=nerve conduction studies. PE=plasma exchange. POEMS=polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes. *Almost no impairment and disability, and no effect on daily life, no axon loss. †Mild to moderate impairment and disability, no serious effect on daily life (the patient can work or has near normal social life). ‡Moderate to severe impairment or disability, clear effect on daily life, active axon loss.

TREAMENT OPTIONS (CLASS IV EVIDENCE)

Table 3 Immunosuppressant and immunomodulatory drugs that have been reported to be beneficial in chronic inflammatory demyelinating polyradiculoneuropathy (Class IV evidence [29,41])

- Alemtuzemab
- Azathioprine
- Cyclophosphamide
- Ciclosporin
- Etanercept
- Interferon-α
- Interferon-β1a
- Mycophenolate mofetil
- Methotrexate
- Rituximab
- Stem cell transplantation (haematopoietic)

Journal of Neurology
https://doi.org/10.1007/s00415-018-8948-y

ORIGINAL COMMUNICATION

Corticosteroids in chronic inflammatory demyelinating polyneuropathy

A retrospective, multicentre study, comparing efficacy and safety of daily prednisolone, pulsed dexamethasone, and pulsed intravenous methylprednisolone

G. G. A. van Lieverloo[1] · S. Peric[2] · P. E. Doneddu[3] · F. Gallia[3] · A. Nikolic[2] · L. Wieske[1] · C. Verhamme[1] · I. N. van Schaik[1] · E. Nobile-Orazio[3] · I. Basta[2] · F. Eftimov[1]

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Table 1 Patients characteristics at baseline per treatment group

	Prednisolone	Dexamethasone	Methylprednisolone	Total	*p* value
Inclusion, *N* (%)	67 (54%)	37 (30%)	21 (17%)	125 (100%)	
The Netherlands	6	37	0	43	
Serbia	57	0	1	58	
Italy	4	0	20	24	
Male, *N* (%)	41 (61%)	29 (78%)	15 (71%)	85 (68%)	0.18
Mean age (SD)	51.1 (18)	55.6 (14)	57.1 (14)	53.4 (16)	0.20
Walking unassisted, *N* (%)	47 (70%)	33 (89%)	20 (95.5%)	100 (80%)	0.01[a]
Median MRC sum score (range)	50 (34–60)	56 (46–60)	57 (42–60)	53 (34–60)	0.003[a]
CIDP subtype, *N* (%)	Typical: 58 (87%) Atypical: 9 (13%) (MADSAM 3, DADS 2, pure motor 4)	Typical: 28 (76%) Atypical: 9 (24%) (MADSAM 5, pure sensory 3, pure motor 1)	Typical: 12 (57%) Atypical: 9 (43%) (MADSAM 4, DADS 2, pure sensory 3)	Typical: 98 (78%) Atypical: 27 (22%) (MADSAM 12, DADS 4, pure sensory 6, pure motor 5)	0.03[a]

MRC Medical Research Council sum score (six paired muscle groups), *MADSAM* multifocal acquired demyelinating sensory and motor neuropathy, *DADS* distal-acquired demyelinating symmetric polyneuropathy

[a]Post hoc analysis

Table 2 Response rate per treatment group and median duration of treatment in treatment responders

	Prednisolone N=67	Dexamethasone N=37	MPS N=21	Total N=125	*p* value
Treatment response					
Responder, *N* (%) (95% CI)	38 (57%) (45–69%)	25 (68%) (52–83%)	12 (57%) (34–80%)	75 (60%) (51–69%)	0.56
Median duration of treatment (responders only)					
In months (range)	15 (2–90)	6 (5–12)	6.5 (1–60)	6 (2–90)	
Estimated cumulative dose, converted to prednisolone					
Based on 80 kg bodyweight[a]	10800 mg[a]	6000 mg	9375 mg		

MPS methylprednisolone
[a]Based on 80 kg bodyweight

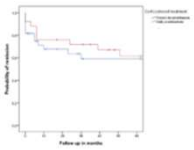
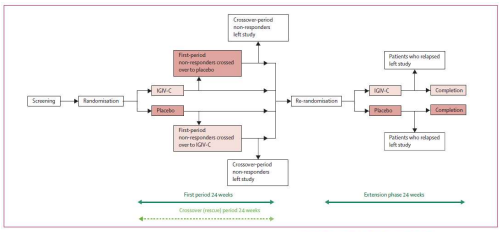


Table 3 Proportion of patients in remission and median time to relapses in treatment responders

Treatment responders	Prednisolone N=38	Dexamethasone N=25	MPS N=12	Total N=75	*p* value
Patients in remission, *N* (%) (95% CI)	25 (66%) (50–82%)	16 (64%) (44–84%)	5 (42%) (9–74%)	46 (61%) (50–73%)	0.343
Median follow-up of patients reaching remission (range in months)	31 (1–180)	93 (17–197)	19 (2–45)	55 (1–197)	
Median time to relapse (range in months)	0 (0–30)	6 (0–51)	0 (0–12)	4 (0–51)	
< 6 months, *N*	9	6	3	20	
> 6 months, *N* (range in months)	4 (7–30)	3 (24–51)	2 (6–12)	9 (7–51)	

Intravenous immune globulin (10% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomised placebo-controlled trial

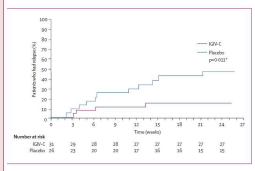


Lancet Neurol 2008; 7: 136-44

	IGIV-C (n=59)	Placebo (n=58)
Sex		
Male	31 (53%)	46 (79%)
Female	28 (47%)	12 (21%)
Age (years)		
Mean	50 (17)	53 (16)
Range	19-79	18-83
Ethnic origin		
White	55 (93%)	52 (90%)
Black	0	1 (2%)
Hispanic	3 (5%)	5 (9%)
Other	1 (2%)	0
Previous IVIg treatment	20 (34%)	12 (21%)
Time since first CIDP symptoms (years)	5·8 (7·4)	4·8 (4·9)
Time since CIDP diagnosis (years)	3·4 (3·7)	1·8 (2·9)
Baseline INCAT disability score	4·2 (1·4)	4·1 (1·5)
Baseline amplitude (mV)*	1·29 (1·39)	1·82 (1·99)
Baseline grip strength (kPa)		
Dominant hand	48·2 (23·6)†	52·1 (23·3)
Non-dominant hand	47·0 (25·1)†	50·2 (22·8)
Baseline MRC sum score	49·3 (6·9)	50·0 (7·2)
Baseline ISS score	7·8 (4·9)†	7·9 (4·9)†

Data are number (%) or mean (SD) unless otherwise indicated. *Baseline action potential amplitude of the most severely affected motor nerve at most proximal site. †n=57. ‡n=58.

Table 1: First-period demographics and baseline characteristics



ICE STUDY: IVIG VS PLACEBO

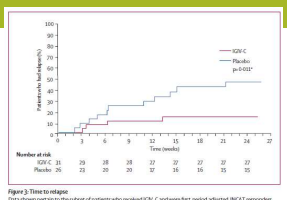
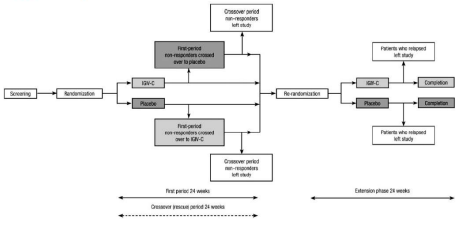


Figure 3: Time to relapse
Data shown pertain to the subset of patients who received IGIV-C and were first-period adjusted-INCAT responders (showed and maintained an improvement of ≥ 1 point relative to baseline). These patients were followed for time to relapse (ie, a decrease in adjusted INCAT score of ≥ 1 point that was not attributed to a change of 0 to 1 in the upper extremities) during the extension phase. The patient who was enrolled in the extension phase in error was not included in the analysis. *p for difference between groups.

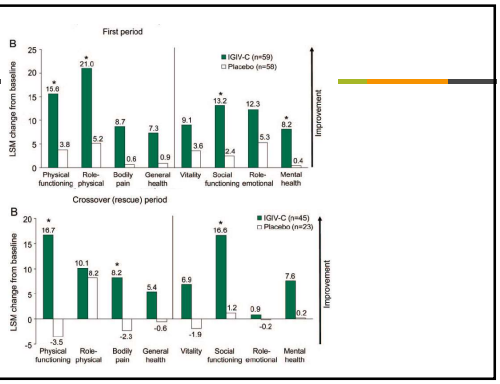
Lancet Neurol 2008; 7: 136-44

NEUROLOGY Health-related quality-of-life improvements in CIDP with immune globulin IV 10%

Figure 1 Study design



Neurology 2009;72:1337-1344



LONG-TERM OUTCOME IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY PATIENTS TREATED WITH INTRAVENOUS IMMUNOGLOBULIN: A RETROSPECTIVE STUDY

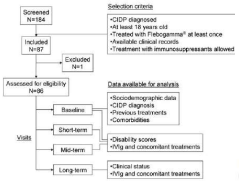


FIGURE 1. Flow of patients and data available for analysis.

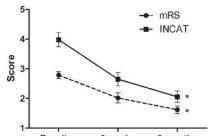


FIGURE 2. mRS and INCAT score evolution from baseline to mid-term visit ($^*P < 0.001$). Values are presented as mean ± SEM.

Muscle Nerve 48: 870–876, 2013

LONG-TERM OUTCOME IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY PATIENTS TREATED WITH INTRAVENOUS IMMUNOGLOBULIN: A RETROSPECTIVE STUDY

Eighty-six patients were included;

- 60.5% responded at short term and 54.6% at midterm.
- At long term, 25.6% of patients were in remission, 65.1% were stable, and 9.3% were non-responders.
- The only variable associated with remission was a better response during the first 6 months of follow-up.

Conclusions: A significant percentage of patients did not require any additional drugs in the long term.

- This suggests that treatment effect or disease outcome may be stable over time, and treatment regimens should therefore be individualized to avoid overtreatment.

Muscle Nerve 48: 870–876, 2013

NEUROLOGY

Single nucleotide polymorphism of TAG-1 influences IVIg responsiveness of Japanese patients with CIDP

Neurology 2009;73:1348-1352

Predicting treatment responses to IV immunoglobulins

Can we already ask the genes?

Neurology 2009;73:1344-1345

Intravenous immunoglobulin versus intravenous methylprednisolone for chronic inflammatory demyelinating polyradiculoneuropathy: a randomised controlled trial

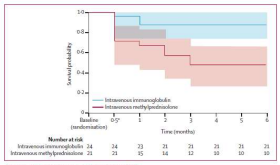


Figure 2: Time to failure occurrence (actuarial method)
Product-limit survival estimates with number of patients at risk and 95% CIs (shaded areas). *0·5 months–35 days.

Interpretation Treatment of CIDP with IVIg for 6 months was less frequently discontinued because of inefficacy, adverse events, or intolerance than was treatment with intravenous methylprednisolone. The longer-term effects of these treatments on the course of CIDP need to be addressed in future studies.

The proportion of patients with adverse events did not differ between the intravenous methylprednisolone group (14 (67%) of 21) and the IVIg group (11 (46%) of 24; p=0.1606).
After therapy discontinuation, more patients on IVIg worsened and required further therapy (eight (38%) of 21) than did those on methylprednisolone (none of ten; p=0.0317).

Lancet Neurol 2012; 11: 493–502

Pulsed high-dose dexamethasone versus standard prednisolone treatment for chronic inflammatory demyelinating polyradiculoneuropathy (PREDICT study): a double-blind, randomised, controlled trial

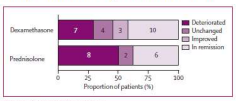


Figure 2: Remission at 12 months
Odds ratio for proportion of patients who deteriorated 2·43 (95% CI 0·7–9·1).

Lancet Neurol 2010; 9: 245–53

	Total study population (n=40)	Dexamethasone (n=24)	Prednisolone (n=16)	OR (95% CI)
Reached primary outcome	16	10	6	1·19 (0·3–4·4)
No remission	24	14	10	-

Data are n or OR (95% CI). Each relapse during the follow-up period has been considered as a treatment failure and excludes the possibility of a remission at 12 months. OR=odds ratio.

Table 3: Primary outcome measure

Interpretation Pulsed high-dose dexamethasone treatment did not induce remission more often than prednisolone treatment. A substantial proportion of patients were in remission at 12 months in both treatment groups. High-dose dexamethasone could be considered as induction therapy in CIDP, but comparison with intravenous immunoglobulin treatment is needed.

INTRAVENOUS IMMUNOGLOBULIN FOR CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY.

- The evidence from randomised controlled trials shows that intravenous immunoglobulin improves disability for at least two to six weeks compared with placebo,
- Number needed to treat of 3.00
- During this period it has similar efficacy to plasma exchange and oral prednisolone.
- In one large trial, benefit of IVIg persisted for 24 and possibly 48 weeks.

Cochrane Database Syst Rev 2009;(1):CD001797.

SUBCUTANEOUS IMMUNOGLOBULIN THERAPY FOR MULTIFOCAL MOTOR NEUROPATHY.

- MMN treated with intravenous immunoglobulin (IVIg) were switched to weekly SCIg in a single-center, open-label pilot intervention study.
  - First group :SCIg dose equivalent to 50% of the IVIg maintenance dose. In case of deterioration, patients received a loading dose of IVIg and doubling of SCIg dose.
  - Second group started with a dose equivalent to the IVIg maintenance dose.
- Outcomes:
  - Primary outcome was the Medical Research Council (MRC) sum score from 10 muscle groups. Secondary outcomes were grip and pinch strength, dexterity, disability, quality of life, adverse events, and serum immunoglobulin concentrations.
- Results: Ten patients were included, five in both groups.
  - In the first group, one patient withdrew , four deteriorated.
  - In the second group, four out of five patients maintained muscle strength with SCIg during the 6 months follow-up. Local adverse events were frequent, especially during first weeks of treatment, but generally well tolerated.
  - Seven mild systemic adverse events were reported, all but one in the first week of treatment. In some, but not all MMN patients in this study,
- SCIg therapy was feasible and safe and maintained strength as well as IVIg. SCIg may be a viable alternative maintenance therapy in some patients with MMN currently receiving IVIg.

J Peripher Nerv Syst 2009 14:93-100.

Clin Drug Investig
DOI 10.1007/s40261-016-0401-3

ORIGINAL RESEARCH ARTICLE

Economic Evaluation of Intravenous Immunoglobulin plus Corticosteroids for the Treatment of Steroid-Resistant Chronic Inflammatory Demyelinating Polyradiculoneuropathy in Thailand

Naruemon Bamrungsawad[1] · Nilawan Upakdee[1] · Chayanin Pratoomsoot[2] · Rosarin Srisamsiri[3] · Piyameth Dilokthornsakul[2,3] · Supinya Dechanont[1] · David Bin-Chia Wu[4] · Charungthai Dejthevaporn[5] · Nathorn Chaiyakunapruk[1,3,4,6,7]

Published online: 25 April 2016

RESULT

Incremental cost-effectiveness ratio (ICER) of US$1672.71 per QALY gained.

At a threshold of US$4672 per QALY gained, IVIG plus corticosteroids is considered a cost-effective treatment for steroid-resistant CIDP patients in Thailand.

Systematic review of rituximab for autoimmune diseases: a potential alternative to intravenous immune globulin

TABLE 1. Description of rituximab studies: randomized trials and observational st

Studies	Disease	Number or range	Rituximab
Randomized trials			
Gudbrandsdottir et al., 2013[45]	ITP	124	375 mg/m² weekly × 4 doses
Ghanima et al., 2015[47]	ITP	109	375 mg/m² weekly × 4 doses
Zaja et al., 2010[20,37]	ITP	101	375 mg/m² weekly × 4 doses
Li et al., 2012[37]	ITP	62	100 mg weekly × 4 doses
Arnold et al., 2012[17]	ITP	58	375 mg/m² weekly × 4 doses
Merrill et al., 2010[48]	SLE	257	1 g every 2 weeks × 2 doses
Rovin et al., 2012[18]	SLE	144	1 g every 2 weeks × 2 doses
Dass et al., 2008[49]	Sjogren's syndrome	17	1 g every 2 weeks × 2 doses
Devauchelle-Pensec et al., 2014[19]	Sjogren's syndrome	120	1 g every 2 weeks × 2 doses
Observational studies (number of studies)			
38	ITP	12-248	Variable doses
24	SLE	10-169	Variable doses
20	Pemphigus vulgaris	10-92	Variable doses
7	Sjogren's syndrome	11-74	Variable doses
4	Myasthenia gravis	11-132	375 mg/m² weekly × 4 doses
2	CIDP	13-18	375 mg/m² weekly × 4 doses

RXT = rituximab; SOC = standard of care.

TRANSFUSION 2018;58:2729–2735

Systematic review of rituximab for autoimmune diseases: a potential alternative to intravenous immune globulin

TABLE 3. Pooled response rates with rituximab for each disease subgroup from observational studies

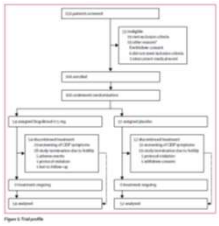
Condition	Response rate (95% CI)
Pemphigus vulgaris	94% (88%-98%)
Myasthenia gravis	77% (59%-91%)
SLE	69% (59%-78%)
ITP	64% (58%-70%)
Sjogren's syndrome	54% (33%-74%)
CIDP	48% (30%-66%)

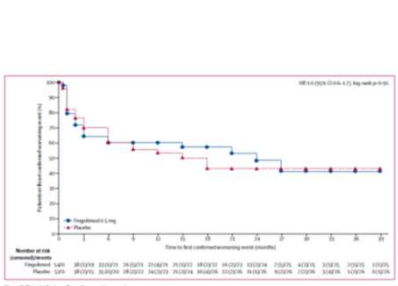
TRANSFUSION 2018;58:2729–2735

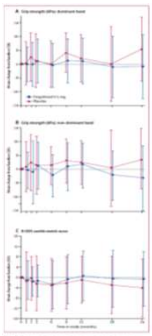
Oral fingolimod for chronic inflammatory demyelinating polyradiculoneuropathy (FORCIDP Trial): a double-blind, multicentre, randomised controlled trial

Lancet Neurol 2018; 17: 689–98

Fingolimod, a sphingosine 1-phosphate receptor modulator, has been shown to reduce the rate of relapse, progression of clinical disability, and MRI evidence of inflammatory lesion activity and tissue destruction in relapsing multiple sclerosis,



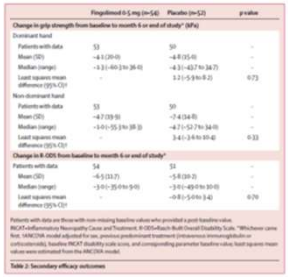




CONCLUSION

Fingolimod 0·5 mg once-daily was not better than placebo for the treatment of CIDP.

Future trial designs should take account of the possibility that if IVIg is stopped abruptly, some patients might relapse soon afterwards whereas others might remain in remission.



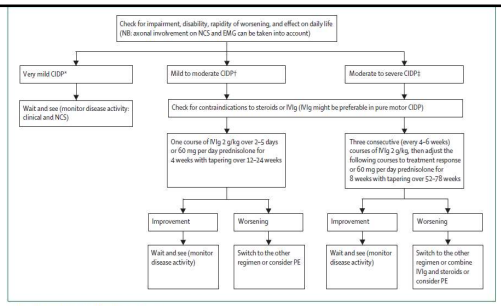
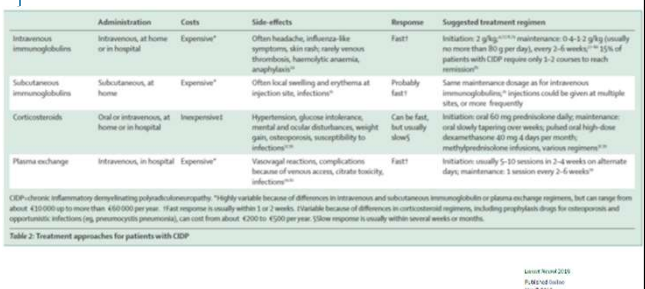


Figure 4: Proposed algorithm for CIDP treatment
At any step, if treatment fails, consider the following diagnoses: POEMS syndrome, lymphoma, amyloidosis, or sarcoidosis. If the patient still worsens under treatment or needs constant treatment maintenance, consider adding an immunosuppressant. CIDP=chronic inflammatory demyelinating polyradiculoneuropathy. EMG=electromyography. IVIg=intravenous immunoglobulin. NCS=nerve conduction studies. PE=plasma exchange. POEMS=polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes. *Almost no impairment and disability, and no effect on daily life, no axon loss. †Mild to moderate impairment and disability, no serious effect on daily life (the patient can work or has near normal social life). ‡Moderate to severe impairment or disability, clear effect on daily life, active axon loss.

TREAMENT OPTIONS (CLASS IV EVIDENCE)

Table 3 Immunosuppressant and immunomodulatory drugs that have been reported to be beneficial in chronic inflammatory demyelinating polyradiculoneuropathy (Class IV evidence [29,41])

Alemtuzemab
Azathioprine
Cyclophosphamide
Ciclosporin
Etanercept
Interferon-α
Interferon-β1a
Mycophenolate mofetil
Methotrexate
Rituximab
Stem cell transplantation (haematopoietic)



	Administration	Costs	Side-effects	Response	Suggested treatment regimen
Intravenous immunoglobulins	Intravenous, at home or in hospital	Expensive*	Often headache, influenza-like symptoms, skin rash, rarely venous thrombosis, haemolytic anaemia, anaphylaxis[30]	Fast†	Initiation: 2 g/kg,[30,31,34,35] maintenance: 0·4–1·2 g/kg (usually no more than 80 g per day), every 2–6 weeks;[31–34] 35% of patients with CIDP require only 1–2 courses to reach remission[30]
Subcutaneous immunoglobulins	Subcutaneous, at home	Expensive*	Often local swelling and erythema at injection site, infections[30]	Probably fast†	Same maintenance dosage as for intravenous immunoglobulins;[30] injections could be given at multiple sites, or more frequently
Corticosteroids	Oral or intravenous, at home or in hospital	Inexpensive‡	Hypertension, glucose intolerance, mental and ocular disturbances, weight gain, osteoporosis, susceptibility to infections[30,36]	Can be fast, but usually slow§	Initiation: oral 60 mg prednisolone daily; maintenance: oral slowly tapering over weeks; pulsed oral high-dose dexamethasone 40 mg 4 days per month; methylprednisolone infusions, various regimens[8,30]
Plasma exchange	Intravenous, in hospital	Expensive*	Vasovagal reactions, complications because of venous access, citrate toxicity, infections[30,36]	Fast†	Initiation: usually 5–10 sessions in 2–4 weeks on alternate days; maintenance: 1 session every 2–6 weeks[30]

CIDP=chronic inflammatory demyelinating polyradiculoneuropathy. *Highly variable because of differences in intravenous and subcutaneous immunoglobulin or plasma exchange regimens, but can range from about €10 000 up to more than €60 000 per year. †Fast response is usually within 1 or 2 weeks. ‡Variable because of differences in corticosteroid regimens, including prophylaxis drugs for osteoporosis and opportunistic infections (eg, pneumocystis pneumonia), can cost from about €200 to €500 per year. §Slow response is usually within several weeks or months.

Table 2: Treatment approaches for patients with CIDP

TABLE 1. Summary of Efficacy of Intravenous IgG in Neuromuscular Diseases Based on the Clinical Trials

Intravenous IgG Treatment in Neuromuscular Diseases	
Guillain-Barre syndrome	First-line treatment; off-label; class I evidence
MMN	First-line treatment; Food and Drug Administration–approved; class I evidence
Chronic inflammatory demyelinating polyneuropathy	First-line treatment; Food and Drug Administration–approved; class I evidence
MG	First-line treatment for MG exacerbation; off-label; short-term efficacy; long-term efficacy has not been established; class I evidence
DM	Second-line treatment for refractory cases; off-label; class I evidence
PM	Off-label; class IV evidence
NAM	Off-label; class IV evidence
IBM	Class I (not effective)
Stiff-person syndrome	First-line treatment; off-label; class I evidence

J Clin Neuromuscular Dis 2019;20:182–193)

การใช้ยาบัญชี จ(2)
(ร่าง) แนวทางกำกับการใช้ยา **intravenous human normal immunoglobulin,**
ข้อบ่งใช้ โรค Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

IVIG AS SECOND LINE TREATMENT

4.4 ผู้ป่วยได้รับ **corticosteroid** หรือ **corticosteroid** ร่วมกับยากดภูมิคุ้มกัน และมีลักษณะทางคลินิกข้อใดข้อหนึ่งดังต่อไปนี้‡

4.4.1 ได้รับยาเป็นเวลา 1 เดือน และมี Inflammatory Neuropathy Cause and Treatment (INCAT) score ≥ 6 (รายละเอียดตามภาคผนวกแนบท้าย) หรือ

4.4.2 ได้รับยาเป็นเวลา 3 เดือน และมี INCAT score ≥ 2 หรือ

4.4.3 มีผลข้างเคียงที่รุนแรงในระดับ grade 3 หรือ 4 จากการใช้ **corticosteroid** หรือ **corticosteroid**ร่วมกับยากดภูมิคุ้มกัน

การใช้ยาบัญชี จ(2)
(ร่าง) แนวทางกำกับการใช้ยา **INTRAVENOUS HUMAN NORMAL IMMUNOGLOBULIN,**
ข้อบ่งใช้ โรค **CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)**

Diagnosis: EFNS criteria

5. ขนาดยาที่แนะนำ และวิธีการให้ยา

5.1 ขนาดยา IVIG ที่แนะนำ คือ 2 กรัมต่อน้ำหนักตัว 1 กิโลกรัม แบ่งให้ 2-5 วัน และตามด้วยขนาด 0.5-1 กรัมต่อน้ำหนักตัว 1 กิโลกรัม แบ่งให้ 1-2 วัน ให้ยาด้วยวิธี **continuous infusion** สามารถให้ IVIG ซ้ำได้ห่างกันอย่างน้อย 4 สัปดาห์ ในกรณีดังต่อไปนี้

- ผู้ป่วยอาการยังไม่ดีขึ้นหรืออาการเลวลง (INCAT score เท่าเดิมหรือเพิ่มขึ้นเมื่อเทียบกับ **baseline**) ภายใน 6 เดือนหลังให้ยา IVIG ครั้งแรก
- ผู้ป่วยอาการดีขึ้นโดยมีค่า INCAT score ลดลงอย่างน้อย 1 คะแนนเมื่อเทียบกับ **baseline** โดยใช้ยาติดต่อกันไม่เกิน 1 ปี

5.2 สามารถใช้ร่วมกับยากดภูมิคุ้มกันอื่นได้

การใช้ยาบัญชี จ(2)
(ร่าง) แนวทางกำกับการใช้ยา **INTRAVENOUS HUMAN NORMAL IMMUNOGLOBULIN,**
ข้อบ่งใช้ โรค **CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP)**

7. เกณฑ์การหยุดยา

7.1 ตอบสนองต่อการรักษา กล่าวคือ INCAT score ลดลงอย่างน้อย 1 คะแนนเมื่อเทียบกับ **baseline** โดยให้ยาต่อเนื่องจนครบ 1 ปี หลังจากเริ่มรักษา

7.2 ไม่ตอบสนองต่อการรักษา กล่าวคือ INCAT score เท่าเดิมหรือเพิ่มขึ้นเมื่อเทียบกับ **baseline** หลังจากได้รับยาไปแล้ว 6 เดือน

7.3 สถานะของผู้ป่วยเปลี่ยนเป็น **terminally ill**

7.4 ผู้ป่วยเกิดอาการข้างเคียงจากการใช้ยา IVIG จนไม่สามารถใช้ยา IVIG ต่อได้

INCAT DISABILITY SCALE

Arm disability
0 No upper limb problems
1 Symptoms, in one or both arms, not affecting the ability to perform any of the following functions: doing all zips and buttons; washing or brushing hair; using a knife and fork together; handing small coins
2 Symptoms, in one arm or both arms, affecting but not preventing any of the above mentioned functions
3 Symptoms, in one arm or both arms, preventing one or two of the above mentioned functions
4 Symptoms, in one arm or both arms, preventing three or all of the functions listed, but some purposeful movements still possible
5 Inability to use either arm for any purposeful movement
Leg disability
0 Walking not affected
1 Walking affected, but walks independently outdoors
2 Usually uses unilateral support (stick, single crutch, one arm) to walk outdoors
3 Usually uses bilateral support (sticks, crutches, frame, two arms) to walk outdoors
4 Usually uses wheelchair to travel outdoors, but able to stand and walk a few steps with help
5 Restricted to wheelchair, unable to stand and walk a few steps with help
Overall disability results from sum of arm and leg disability scores

Hughes R, Bensa S, Willison H, et al. Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol 2001;50:195-201.

Low-quality evidence from randomised trials does not show significant benefit from azathioprine (1 trial) or interferon beta-1a (2 trials)

Moderate quality evidence from one randomised trial does not show significant benefit from a relatively low dose of methotrexate (1trial)

None of the trials was large enough to rule out small or moderate benefit.

The evidence from observational studies is insufficient o avoid the need for randomised controlled trials to discover whether these drugs are beneficial.

Future trials should have improved designs, more sensitive outcome measures relevant to people with CIDP, and longer treatment durations.

No recommendation for cyclophosphamide, rituximab, cyclosporin

SUMMARY OF TREATMENT

Induction

50-80% effective

- Steroid
- Immunoglobulin (IVIg)
- Plasma exchange

Maintenance

- Steroid
- Ig (IV, SC)
- ? AZA, CyA, MMF
- Not effective
- Add on : MTX, fingolimod

STEROID

PO:

- Prednisolone 60 mg per day, then tapering: trial data up to 15 months
- Dexamethasone 40 mg per day for 4 days every 4 weeks: trial data up to 6 months

IV

- pulse methylprednisolone 1000 mg, then weekly or monthly

Pulse oral and IV may have fewer side effect
May have more remission at 6 months when compared to IVIg

PLASMA EXCHANGE

- Not responding to IVIg or steroid case
- 5-10 sessions within 2-4 weeks
- Not practical for maintenance

IVIG

- IV for induction, IV or SC form maintenance
- 15% remission after 1-2 courses of treatment

WHAT IF THE FIRST LINE FAILS ?

- Second monotherapy: around 60-70 % success rate
- One retrospective study
1. First treatment: 76% success rate in first line IVIg
2. Second treatment in IVIg non responder: 67% success rate with PE, 59% success rate with steroid
3. Third treatment: switch to other treatment: 75% success rate

Don't forget to look for alternative diagnosis !

MAINTENANCE PHASE

- IVIg : should be started in patients who deteriorate after initial improvement with 1-2 courses of IVIg
  - 0.4- 1.2 g/kg/d every 2-6 weeks (not more than 80 g/d)
  - Possible role of serum IVIg concentration as a dosage guide, but variable between patients

SC option in certain situation: home infusion, travel, difficult IV access

OTHER AGENTS: ADD ON THERAPY

Limited data : to reduce the dose of steroid or IVIg

- MTX
- Azathioprine
- Cyclosporin
- Rituximab

IGG4 AB TO NODAL AND PARANODAL PROTEIN

- Common feature : poor response or no response to IVIg , which could be explained by the low capacity to bind with FcγIIb-receptors and inability to activate complement.
- Treatment with corticosteroids and plasma exchange seems partly effective.
- Treatment-refractory patients with CIDP and IgG4 antibodies showed variable responses to rituximab, from no response (mainly in patients with long disease duration and severe axonal damage) to remarkably good responses with clinical recovery and depletion of IgG4 antibodies.
- Future prospective clinical trials on the efficacy of rituximab in patients with CIDP and IgG4 antibodies are needed.

FUTURE STUDIES

- IVIg dose finding cross over trial
- IVIg maintenance dose finding trial
- Combination: IVIg plus IVMP VS IVIg plus placebo
- Other agents
  - Complement inhibitor
  - FcRn blocker
  - Immunoabsorption
  - IgG degrading enzyme of S. pyogenes
  - Rituximab
  - Ocrelizumab

CONCLUSION

- Common and uncommon features
- Diagnostic procedure and criteria
- Clinicopathological association
- Treatment options
  - Immunosuppressive therapy
  - IVIg
  - Comparative data
  - Guideline