Chronic Immune Demyelinating Polyneuropathy (CIDP):
An overview and management update

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University of Saskatchewan

Objectives

- Discuss pathophysiology, clinical features, and diagnosis of CIDP
- Review treatment strategies drawing from recent studies and guidelines
- Discuss practical use of IVIg, SCIg, steroids and other agents in CIDP through use of clinical cases

Disclosures

- Relationships with commercial interests:
  - Grants for Educational Activities: Genzyme, Allergan, Mitsubishi-Tanabe, Roche, Takeda
  - Speakers Honoraria: Genzyme, EMD Serono, Akcea, Takeda, Roche, Biogen, Alexion, Amylyx, CSL Behring
  - Advisory Board: Mitsubishi-Tanabe, Alexion, Roche, Biogen, Akcea, Amylyx, Sanofi Genzyme, Argenx
  - Other: Employee of Saskatchewan Health Region
- I will be discussing IVIg, SCIg, steroids, Rituximab, and other immunosuppressants

Case 1

- 40 F with weakness
- Began 6 months prior to presentation
- Getting worse over time
- Difficulty climbing stairs, foot drop, writing, lifting overhead
- Sometimes trips when walking
- Minimal numbness in toes

Case 1

- Otherwise well
- No meds
- No allergies
- Non-smoker, minimal alcohol
- No family history of neuromuscular disease

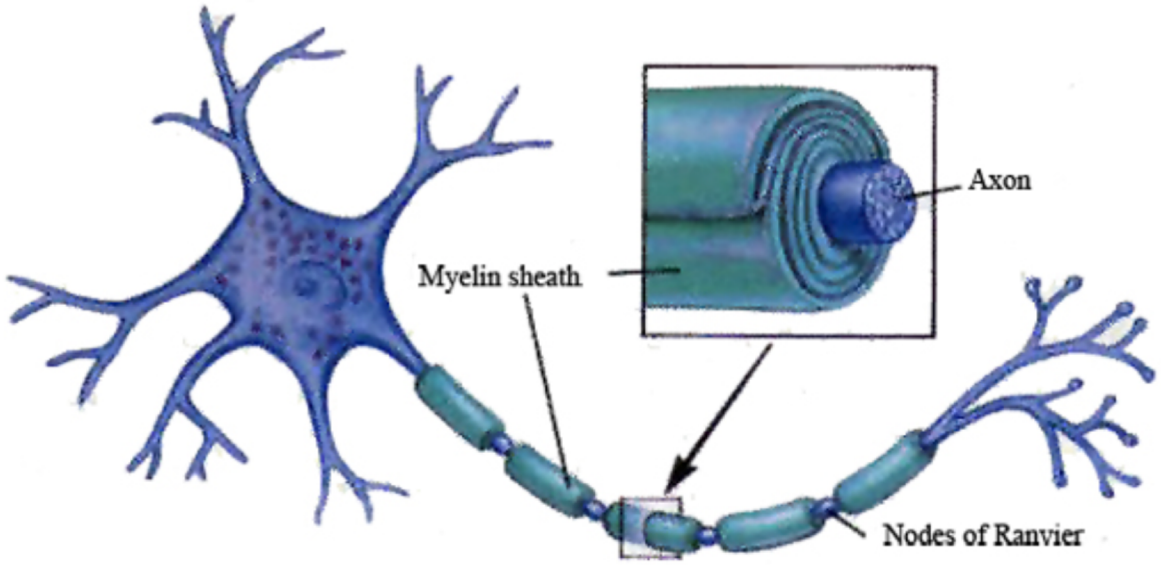
Case 1 Examination

- Normal cranial nerves
- Symmetric weakness
  - Deltoids, biceps, triceps 4/5
  - Hand intrinsic muscles 2-3/5
  - Hip flexion, knee flexion & extension 4+/5
  - Ankle movements 2-3/5
- Reflexes absent
- Mild reduction in vibration & pinprick sensation in feet
- Foot drop when walking

What is CIDP?

Chronic Immune Demyelinating Poly(radiculo)neuropathy

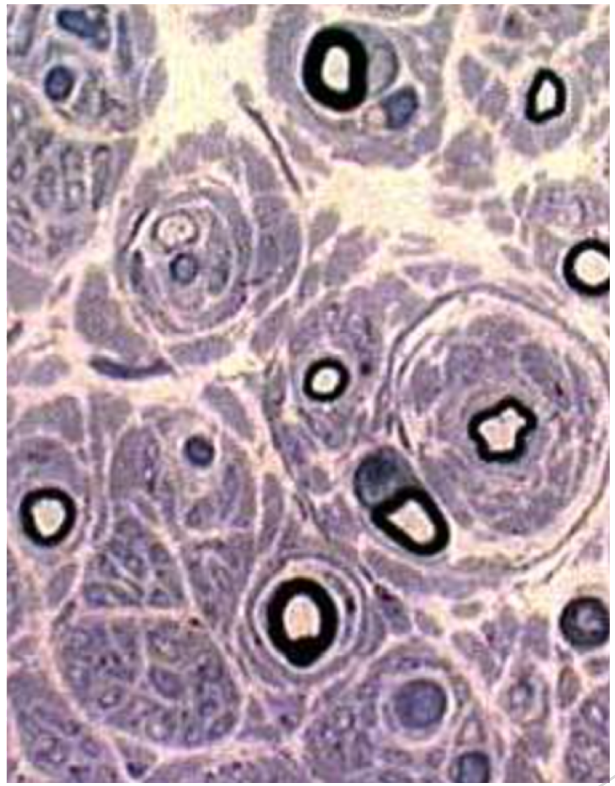
- Immune mediated demyelination of nerves and nerve roots



https://www.google.com/search?q=peripheral+nerve+myelin&safe=active&client=safari&rls=en&tbm=isch&tbas=0&source=lnt&sa=X&ved=0ahUKEwik_cmZ7dLdAhWHzlMKHfrSC1oQpwUIIA&biw=1024&bih=495&dpr=2#imgrc=g9mhmbgIA-6YpM: Accessed September 23, 2018

What is CIDP?

- Immune system activation
  - Cellular - T-cells activated
  - Humoral – Ig deposition on nerve
- Demyelination (segmental) and remyelination
  - Onion bulbs



https://neuromuscular.wustl.edu/pathol/cidppath.htm

What is CIDP?

- Prevalence 1-7/100,000
- Usually presents in adulthood, increases with age
- Somewhat more common in males
- Onset is typically over 8 weeks or more
- May be progressive or relapsing
  - If relapsing, usually in younger patients

What is CIDP?

TABLE 1 Clinical criteria for CIDP

Typical CIDP
All the following: • Progressive or relapsing, symmetric, proximal and distal muscle weakness of upper and lower limbs, and sensory involvement of at least two limbs • Developing over at least 8 weeks • Absent or reduced tendon reflexes in all limbs

Common symptoms in CIDP?

- Proximal muscle weakness
  - Getting up from low seat, lifting arms overhead
- Distal muscle weakness
  - Fine finger movements, foot drop
- Tremor
- Distal numbness +/- pain
  - Vibration, joint position sense

What is CIDP?

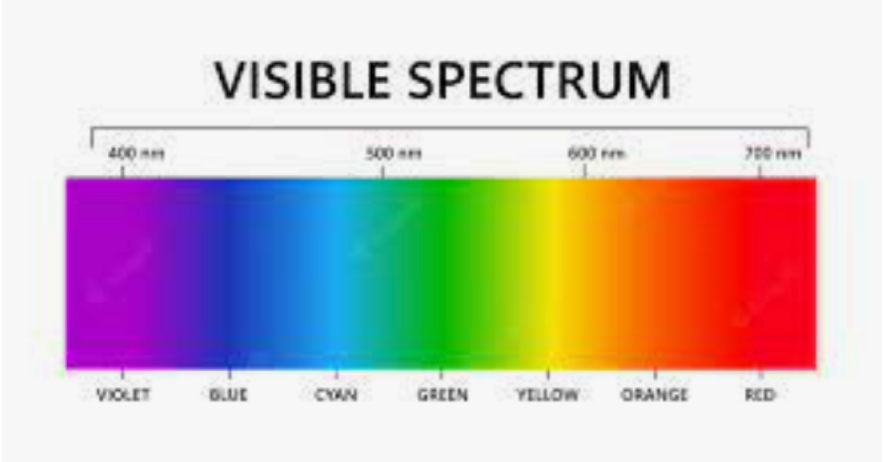
CIDP variants

One of the following, but otherwise as in typical CIDP (tendon reflexes may be normal in unaffected limbs):

- Distal CIDP: distal sensory loss and muscle weakness predominantly in lower limbs
- Multifocal CIDP: sensory loss and muscle weakness in a multifocal pattern, usually asymmetric, upper limb predominant, in more than one limb
- Focal CIDP: sensory loss and muscle weakness in only one limb
- Motor CIDP: motor symptoms and signs without sensory involvement
- Sensory CIDP: sensory symptoms and signs without motor involvement

A Spectrum of Disease

- AIDP aka GBS (Acute)
  - Nadir within 4 weeks
- SAIDP (Subacute)
  - Nadir 4-8 weeks
- CIDP (Chronic)
  - Nadir 8 weeks or more



Case 1

- “Doctor, what’s going on with me? How will you find out?”

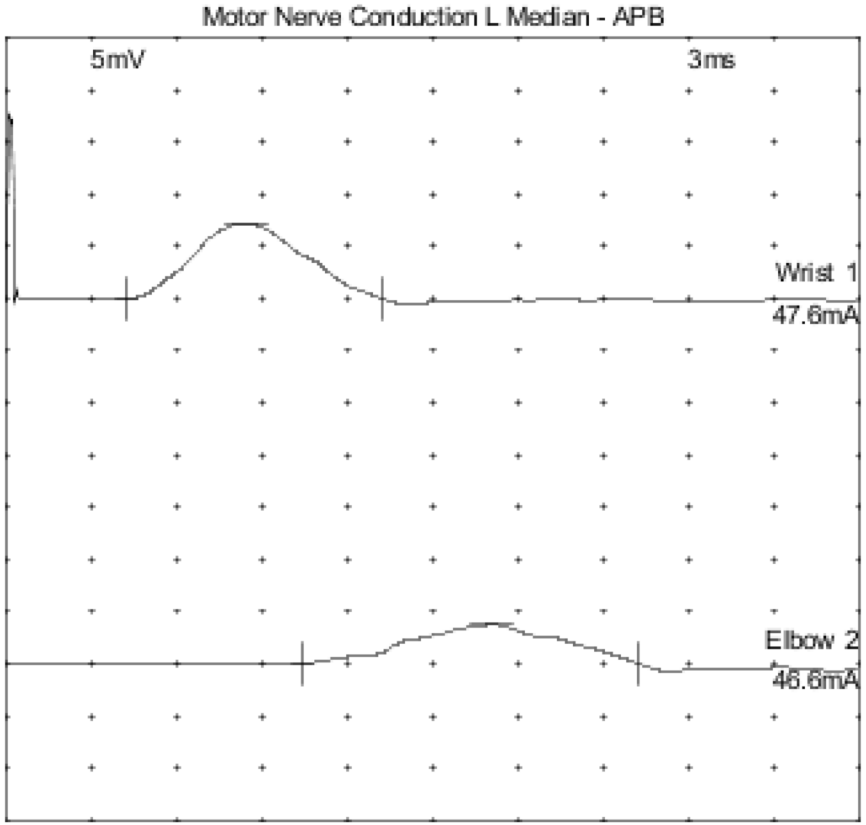
Investigational options

- EMG/NCS (always do)
  - Demyelination
- LP – albuminocytological dissociation (sometimes do)
  - If >10 cells rule out HIV, Lymphoma, Lyme, Sarcoid, etc
- SPEP, UPEP, CBC, fasting glucose, HgbA1c, HIV, creatinine, LFT (always do)
  - Rule out lymphoproliferative disorder, diabetes, HIV, liver & renal disease
  - Can do MANY other labs if atypical features
- Ultrasound or MRI (occasionally do)
  - Enlarged nerve size or increased T2 or Gad enhancement of roots/plexus
- Nerve biopsy (very rarely do)
  - Demyelination seen in 1/2 – 1/3 of cases, but can be useful to rule out other disorders

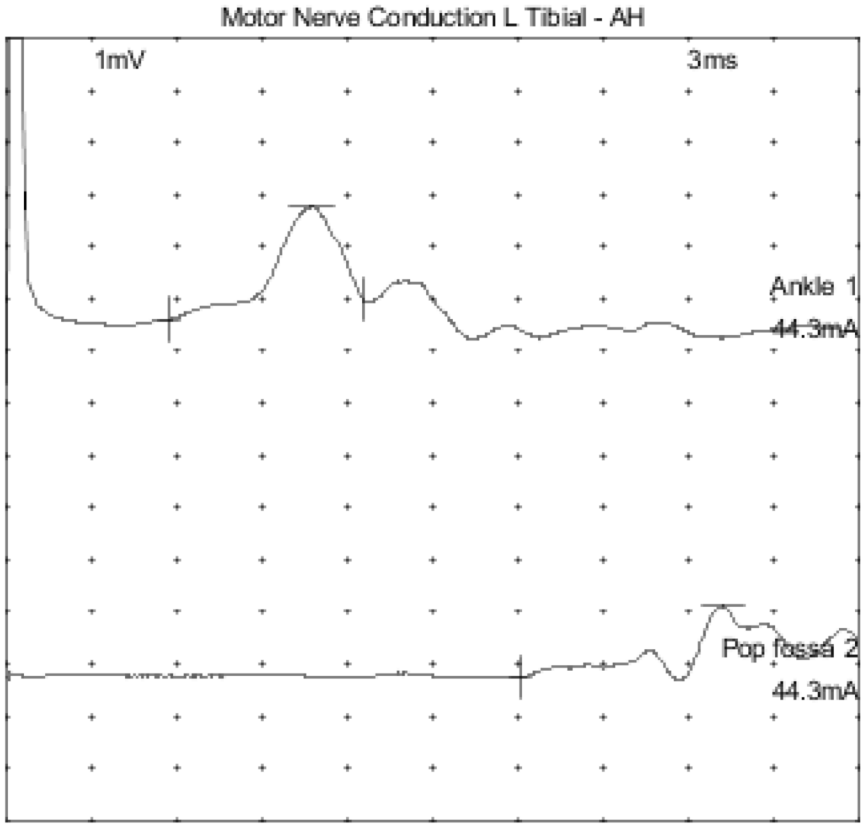
Motor Nerve Conduction

Nerve / Sites	Latency ms	Amplitude mV	Duration ms	Segments	Area mVms	Distance mm	Velocity m/s	Temp. °C
L Median - APB								
Wrist	4.2	7.2	9.0	Wrist - APB	32.2	70		32.6
Elbow	10.4	3.8	11.8	Elbow - Wrist	23.0	203	32.8	
L Ulnar - ADM								
Wrist	3.6	8.0	8.2	Wrist - ADM	38.0	70		
B.Elbow	11.0	4.2	8.5	B.Elbow - Wrist	19.2	207	28.0	
A.Elbow	14.4	2.2		A.Elbow - B.Elbow		101	29.8	
median wrist	NR	NR	NR	median wrist - A.Elbow	NR			
median elbow	NR	NR	NR	median elbow - median wrist	NR			
L Peroneal - EDB								
Ankle	5.7	2.0	9.3	Ankle - EDB	10.0	90		
Fib head	14.7	1.3	9.0	Fib head - Ankle	7.0	290	32.2	
Pop fossa	16.9	1.3	10.5	Pop fossa - Fib head	7.2	81	36.2	
L Tibial - AH								
Ankle	5.7	2.2	6.9	Ankle - AH	4.6	90		
Pop fossa	18.1	1.3		Pop fossa - Ankle		370	29.7	

Conduction block



Temporal dispersion



Sensory Nerve Conduction

Nerve / Sites	Onset Lat ms	Peak Lat ms	Amplitude µV	Segments	Distance mm	Velocity m/s
L Median - Digit II (Antidromic)						
Wrist	2.5	3.4	4.8	Wrist - Dig II	130	52
L Ulnar - Digit V (Antidromic)						
Wrist	2.9	3.9	2.4	Wrist - Dig V	110	38
L Superficial peroneal - Ankle						
Lat leg	3.2	4.1		Lat leg - Ankle	140	43
L Sural - Ankle (Calf)						
Calf	3.2	4.1	5.6	Calf - Ankle	140	44

TABLE 4-10 Motor Nerve Conduction Study Findings Suggesting Demyelination[a]

- Prolongation of distal motor latency ≥50% above the upper limit of normal values
- Reduction of motor conduction velocity ≥30% below the lower limit of normal values
- Prolongation of F-wave latency ≥30% above the upper limit of normal values (≥50% if amplitude of distal negative peak compound muscle action potential [CMAP] is <80% of lower limit of normal values)
- Absence of F waves (only if distal negative peak CMAP amplitude is ≥20% of the lower limit of normal values)
- Partial motor conduction block, defined as ≥50% amplitude reduction of the proximal negative peak CMAP relative to distal (only if the distal negative peak CMAP is ≥20% of the lower limit of normal values)
- Abnormal temporal dispersion, defined as >30% increase in the duration between the proximal and distal negative peak CMAP
- Increased distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak): median ≥6.6 ms, ulnar ≥6.7 ms, peroneal ≥7.6 ms, tibial ≥8.8 ms

[a] Data from Van den Bergh PY, et al, Eur J Neurol.[24] *onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02930.x/full.*

Dimachkie M. & Saperstein D. Acquired Immune Demyelinating Neuropathies. Continuum (Minneap Minn) 2014;20(5):1241–1260.

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Case 1

- Chronic motor > sensory demyelinating symmetric polyneuropathy

Case 1

- Chronic motor > sensory demyelinating symmetric polyneuropathy
  - So, CIDP

Case 1

- Doctor, how will you make me better?”

Treatment options

- IVIg, SCIg
- Steroids
- Plasma exchange
- Immune modulators
  - Rituximab, Azathioprine, Mycophenolate, etc

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GUIDELINES

European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force—Second revision

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Treatment – EFNS Guidelines

- Initial therapy
  - IVIG or steroids
  - PLEX if above are ineffective
- Maintenance therapy
  - SCIg, IVIG, or steroids
  - If refractory or high doses needed, then consider combination therapy or adding an immunosuppressive agent

IVIg = Steroids = PLEX

- Cost
- Side effects
- Supply
- Ease of administration
- Short term & long term benefit

A plasma exchange versus immune globulin infusion trial in chronic inflammatory demyelinating polyradiculoneuropathy.Dyck PJ, Litchy WJ, Kratz KM, Suarez GA, Low PA, Pineda AA, Windebank AJ, Karnes JL, O'Brien PC Ann Neurol. 1994;36(6):838.

Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy.Hughes R, Bensa S, Willison H, Van den Bergh P, Comi G, Illa I, Nobile-Orazio E, van Doorn P, Dalakas M, Bojar M, Swan A, Inflammatory Neuropathy Cause and Treatment (INCAT) Group Ann Neurol. 2001;50(2):195.

Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy.AUEftimov F, Winer JB, Vermeulen M, de Haan R, van Schaik IN SOCochrane Database Syst Rev. 2013;

Treatment

(b) IVIg vs corticosteroids

- Both IVIg and oral or IV corticosteroids are first-line treatments for CIDP. Based on the level of evidence, the TF did not recommend an overall preference for either treatment modality and **weakly recommended either IVIg or corticosteroid treatment.**
- Both short- and long-term effectiveness, risks, ease of implementation, and cost should be considered:
  - IVIg may be preferable when it comes to short-term treatment effectiveness, or when (relative) contraindications for corticosteroids exist.
  - There is some indication that pulsed corticosteroids may be preferable for long-term treatment effectiveness, because of a possible higher rate and longer duration of remission, or when IVIg is unaffordable or unavailable.

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

*Richard A C Hughes, Peter Donofrio, Vera Bril, Marinos C Dalakas, Chunqin Deng, Kim Hanna, Hans-Peter Hartung, Norman Latov, Ingemar S J Merkies, Pieter A van Doorn, on behalf of the ICE Study Group**

Lancet Neurol 2008; 7: 136–44

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See Reflection and Reaction page 115

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Summary

Background Short-term studies suggest that intravenous immunoglobulin might reduce disability caused by chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) but long-term effects have not been shown. We aimed to establish whether 10% caprylate-chromatography purified immune globulin intravenous (IGIV-C) has short-term and long-term benefit in patients with CIDP.

Methods 117 patients with CIDP who met specific neurophysiological inflammatory neuropathy cause and treatment (INCAT) criteria participated in a randomised, double-blind, placebo-controlled, response-conditional crossover trial. IGIV-C (Gamunex) or placebo was given every 3 weeks for up to 24 weeks in an initial treatment period, and patients who did not show an improvement in INCAT disability score of 1 point or more received the alternate treatment in a crossover period. The primary outcome was the percentage of patients who had maintained an improvement from baseline in adjusted INCAT disability score of 1 point or more through to week 24. Patients who showed an improvement and completed 24 weeks of treatment were eligible to be randomly re-assigned in a blinded 24-week extension phase. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00220740.

Findings During the first period, 32 of 59 (54%) patients treated with IGIV-C and 12 of 58 (21%) patients who received placebo had an improvement in adjusted INCAT disability score that was maintained through to week 24 (treatment difference 33·5%, 95% CI 15·4–51·7; p=0·0002). Improvements from baseline to endpoint were also recorded for grip strength in the dominant hand (treatment difference 10·9 kPa, 4·6–17·2; p=0·0008) and the non-dominant hand (8·6 kPa, 2·6–14·6; p=0·005). Results were similar during the crossover period. During the extension phase, participants who continued to receive IGIV-C had a longer time to relapse than did patients treated with placebo (p=0·011). The incidence of serious adverse events per infusion was 0·8% (9/1096) with IGIV-C versus 1·9% (11/575) with placebo. The most common adverse events with IGIV-C were headache, pyrexia, and hypertension.

Interpretation This study, the largest reported trial of any CIDP treatment, shows the short-term and long-term efficacy and safety of IGIV-C and supports use of IGIV-C as a therapy for CIDP.

IVIG – ICE trial

- 2008
- Randomized double blind placebo controlled trial
- N=117
- IVIG vs placebo x 24 weeks
  - IVIG 2g/kg loading, then 1g/kg q 3 weeks
  - If no improvement, got the other treatment in the crossover period
  - If improved, then reassigned in 24 week blinded extension phase
- Most common side effects: headache, fever, high BP

IVIG – ICE trial

- Better disability scores
- Improved hand grip
- Fewer relapses
  - 13% treatment group vs 45% in placebo group

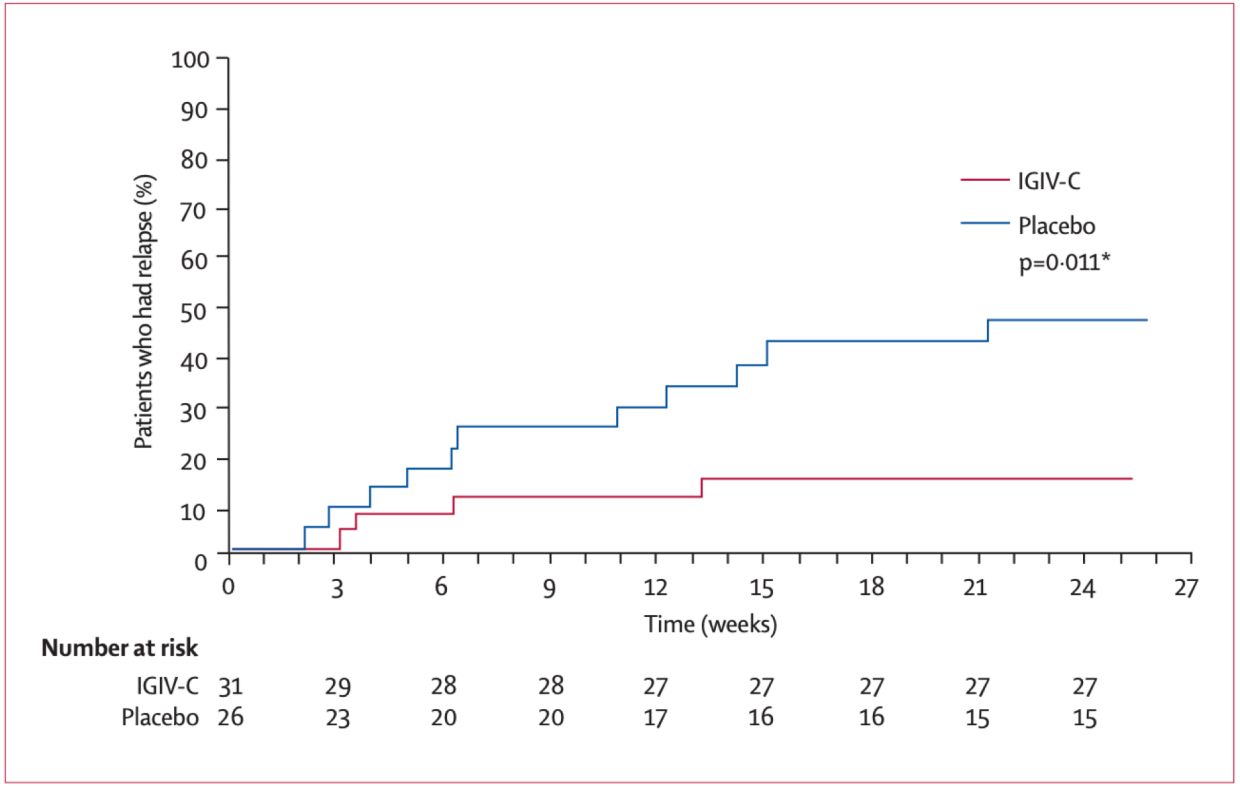

Figure 3: **Time to relapse**
Data shown pertain to the subset of patients who received IGIV-C and were first-period adjusted-INCAT responders (showed and maintained an improvement of ≥1 point relative to baseline). These patients were followed for time to relapse (ie, a decrease in adjusted INCAT score 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.

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Criteria for the Clinical Use of Immune Globulin

Second Edition

February 2022

University of Saskatchewan

✓ Chronic inflammatory demyelinating polyneuropathy (CIDP)

Recommendation includes but is not limited to	○ Demyelinating neuropathy associated with IgG and IgA paraproteinemia
Do Recommendation	IVIG is recommended for first-line treatment, to be initiated when progression is rapid, walking is compromised, or there is significant functional impairment. The diagnosis of CIDP is complicated, particularly in patients with concurrent diabetes. Evaluation by a neurologist with expertise in neuromuscular disease is required.
Dose	Induction: 2 g/kg adjusted body weight divided over 2 to 5 days. Maintenance: 1 g/kg adjusted body weight divided over 1 to 5 days (maximum 1 g/kg/day), every 3 to 4 weeks. SCIG should be considered as an alternative to IVIG following stabilization with IVIG. IVIG should be administered for 3 to 6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles. Some patients may require a higher maintenance dose. Once the patient's condition has stabilized, consider titrating the dose and/or the treatment interval to the lowest dose necessary to maintain clinical effectiveness.
Review Criteria	Continued use of IVIG should be based on objective measures of effectiveness established at the outset of treatment, in consultation with a neurologist. For stable patients, these measures should be assessed, in consultation with a neurologist, no later than 6 months after initiation of long-term treatment and at least annually thereafter. If clinical effectiveness has not been achieved or sustained, IVIG should be discontinued.
Evidence Source	SR (G1); EO (GDG)

Steroids

- Best regimen is not known
- Oral Prednisone
  - Example: 40-60 mg daily tapered over 6-8 months
- Pulsed steroids
  - Example: Solumedrol IV 500mg 4 days per month x 6 months
  - Several trials of either oral DXM or IV Solumedrol
  - Pulsed likely has fewer side effects and better response than daily dosing

Steroids

- Side effect profile might preclude use for some
- Monitor for side effects
  - Diabetes, hypertension, gastric irritation/reflux, cataracts, glaucoma, osteoporosis, avascular necrosis of the hip
- Motor only variants can worsen with steroids
- Some evidence to suggest better long term reduction in relapse rate and cheaper than IVIG
- Try tapering regularly!

Plasma Exchange

- Usually used if patients don't respond to either IVIg or Steroids
- Limited by need for central line & logistics
  - Side effects thrombosis, infection
- Can be considered for patients who are very weak
- Example regimen:
  - 2x/week for 3 weeks, then weekly x 3 wks

Treatment response

- Vast majority improve
- Usually takes 3 months for maximal improvement
  - 90% of those that improve do so after 3 months (ICE trial)
- If stable after for 6 months try to lower or stop
  - 11% will achieve cure (>5y stability off treatment)
  - 20% in remission (stable off treatment <5y)
  - Over 40% stable but need ongoing treatment
  - 5% refractory to treatment

Chronic inflammatory demyelinating polyneuropathy disease activity status: recommendations for clinical research standards and use in clinical practice.Gorson KC, van Schaik IN, Merkies IS, Lewis RA, Barohn RJ, Koski CL, Cornblath DR, Hughes RA, Hahn AF, Baumgarten M, Goldstein J, Katz J, Graves M, Parry G, van Doorn PA J Peripher Nerv Syst. 2010 Dec;15(4):326-33.

Case 1

- After 6 months of IVIg, patient no longer reports any weakness
- On exam
  - Detoids, biceps, triceps, wrist and finger flexors & extensors 5/5
  - Hand intrinsics 4+/5
  - Hip flexion 4+, otherwise legs 5/5
  - Remains areflexic
  - Normal sensation

Case 1

- Reduced IVIG but had re-emergence of weakness
- Resumption of previously effective dose improved examination again.
  - Still some mild weakness on exam but no functional limitations

Case 1

- “Doctor, these IVIG appointments are interfering with my work schedule. Is there something else we can do?”

Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial

*Ivo N van Schaik, Vera Bril, Nan van Geloven, Hans-Peter Hartung, Richard A Lewis, Gen Sobue, John-Philip Lawo, Michaela Praus, Orell Mielke, Billie L Durn, David R Cornblath, Ingemar S J Merkies, on behalf of the PATH study group**

Summary

Background Approximately two-thirds of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) need long-term intravenous immunoglobulin. Subcutaneous immunoglobulin (SCIg) is an alternative option for immunoglobulin delivery, but has not previously been investigated in a large trial of CIDP. The PATH study compared relapse rates in patients given SCIg versus placebo.

Methods Between March 12, 2012, and Sept 20, 2016, we studied patients from 69 neuromuscular centres in North America, Europe, Israel, Australia, and Japan. Adults with definite or probable CIDP who responded to intravenous immunoglobulin treatment were eligible. We randomly allocated participants to 0·2 g/kg or 0·4 g/kg of a 20% SCIg solution (IgPro20) weekly versus placebo (2% human albumin solution) for maintenance treatment for 24 weeks. We did randomisation in a 1:1:1 ratio with an interactive voice and web response system with a block size of six, stratified by region (Japan or non-Japan). The primary outcome was the proportion of patients with a CIDP relapse or who were withdrawn for any other reason during 24 weeks of treatment. Patients, caregivers, and study personnel, including those assessing outcomes, were masked to treatment assignment. Analyses were done in the intention-to-treat and per-protocol sets. This trial is registered with ClinicalTrials.gov, number NCT01545076.

Findings In this randomised, double-blind, placebo-controlled trial, we randomly allocated 172 patients: 57 (33%) to the placebo group, 57 (33%) to the low-dose group, and 58 (34%) to the high-dose group. In the intention-to-treat set, 36 (63% [95% CI 50–74]) patients on placebo, 22 (39% [27–52]) on low-dose SCIg, and 19 (33% [22–46]) on high-dose SCIg had a relapse or were withdrawn from the study for other reasons (p=0·0007). Absolute risk reductions were 25% (95% CI 6–41) for low-dose versus placebo (p=0·007), 30% (12–46) for high-dose versus placebo (p=0·001), and 6% (–11 to 23) for high-dose versus low-dose (p=0·32). Causally related adverse events occurred in 47 (27%) patients (ten [18%] in the placebo group, 17 [30%] in the low-dose group, and 20 [34%] in the high-dose group). Six (3%) patients had 11 serious adverse events: one (2%) patient in the placebo group, three (5%) in the low-dose group, and two (3%) in the high-dose group; only one (an acute allergic skin reaction in the low-dose group) was assessed to be causally related.

Interpretation This study, which is to our knowledge, the largest trial of CIDP to date and the first to study two administrations of immunoglobulins and two doses, showed that both doses of SCIg IgPro20 were efficacious and well tolerated, suggesting that SCIg can be used as a maintenance treatment for CIDP.

Funding CSL Behring.

Lancet Neurol 2017

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SCIg

- 2/3 need long term Ig
- SCIg previously successfully used in immunodeficiencies
- PATH trial (2017)
  - 172 patients
  - SCIg 0.2g/kg or 0.4g/kg weekly vs placebo for 24 weeks
  - More relapses/withdrawals in placebo group
  - ARR 25% for low dose and 30% high dose
  - Only 1 causally related serious adverse event (skin rash)

	Placebo	Low-dose SCIg	High-dose SCIg	Overall p value*	Low-dose SCIg *vs* placebo		High-dose SCIg *vs* placebo		High-dose SCIg *vs* low-dose SCIg	
					Hazard ratio	p value†	Hazard ratio	p value†	Hazard ratio	p value†
Primary outcome	63·2% (50·9–75·4)	39·0% (27·7–53·1)	33·7% (22·8–47·8)	0·0002	0·49 (0·29–0·84)	0·007	0·38 (0·22–0·67)	0·0005	0·80 (0·43–1·49)	0·48
Relapse	58·8% (46·1–72·0)	35·0% (23·9–49·3);	22·4% (12·9–37·2)	<0·0001	0·48 (0·27–0·85)	0·009	0·25 (0·12–0·49)	<0·0001	0·53 (0·25–1·12)	0·09

Data in parentheses are 95% CIs. Data are Kaplan-Meier estimates. All tests are one-sided, with significance defined at a p value of less than 0·025. SCIg=subcutaneous immunoglobulin. *Log-rank test for trend. †Regular log-rank test.

Table 3: **Probability of primary outcome or relapse at 24 weeks**

SCIg

- Near steady state
  - Can use doses weekly, divided over the week, or bi-weekly
  - Open label studies show less hemolytic anemia, nausea, headache
- Straightforward conversion from IVIG
  - Start 1 week post IVIG
  - Divide monthly IVIG dose into weekly dose (or permutation)
  - 1 gram IVIG = 1 gram SCIG
- Taper to lowest effective dose

Markvardsen LH, Christiansen I, Andersen H, Jakobsen J. Headache and nausea after treatment with high-dose subcutaneous versus intravenous immunoglobulin. *Basic Clin Pharmacol Toxicol* 2015; **117:** 409–12.
6 Markvardsen LH, Christiansen I, Harbo T, Jakobsen J. Hemolytic anemia following high dose intravenous immunoglobulin in patients with chronic neurological disorders. *Eur J Neurol* 2014; **21:** 147–52.
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Case 1

- “I feel great! Thanks!”

Case 1

- “I feel great! Thanks!”
- But what if she doesn’t…

If refractory

- Try a different first line agent
- Reconsider your diagnosis
- Combine treatments
- Add an immunosuppressant
  - Azathiorpine, mycophenolate, rituximab, (cyclosporine)
  - Rituximab preferentially if anti-nodal antibodies

Pain

- 20-40% in studies
- Rule out non-neuropathic etiologies
  - Joint issues
- Use antineuralgics
  - Amitriptyline, Gabapentin or Pregabalin, Duloxetine or Effexor
- Don’t use immune treatment primarily for pain

CIDP diagnostic pitfalls and perception of treatment benefit

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ABSTRACT

Objective: We aimed to explore the diagnosis and misdiagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) and to identify pitfalls that erroneously lead to a misdiagnosis.

Methods: A retrospective study of 59 consecutive patients referred with a diagnosis of CIDP was performed. Patients were classified as having or not having CIDP according to European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria. Diagnostic and treatment data were compared in the 2 groups.

Results: Forty-seven percent of patients referred with a diagnosis of CIDP failed to meet minimal CIDP diagnostic requirements. All misdiagnosed patients who satisfied EFNS/PNS clinical criteria would be considered atypical as defined by the EFNS/PNS. CSF cytoalbuminologic dissociation was present in 50% of those without CIDP, although protein elevations were generally mild. Nerve conduction studies in patients without CIDP were heterogeneous, but generally showed demyelinating features better explained by a process other than CIDP. Patients frequently reported improvements after being treated with immunotherapy, even if the CIDP diagnosis was incorrect.

Conclusions: CIDP misdiagnosis is common. Over-reliance on subjective patient-reported perception of treatment benefit, liberal electrophysiologic interpretation of demyelination, and placing an overstated importance on mild or moderate cytoalbuminologic dissociation are common diagnostic errors. Utilization of clear and objective indicators of treatment efficacy might improve our ability to make informed treatment decisions. ***Neurology*® 2015;85:498–504**

Pitfalls in CIDP

- 47% of patients misdiagnosed with CIDP
  - Watch out for concurrent **diabetes** or other diagnoses
- Among those who did NOT have CIDP
  - 85% subjective improvement post IVIG
  - 19% objective improvement
  - ”Subjective patient experiences after IVIG may contribute to CIDP misdiagnosis”
  - Re-examine patients frequently!

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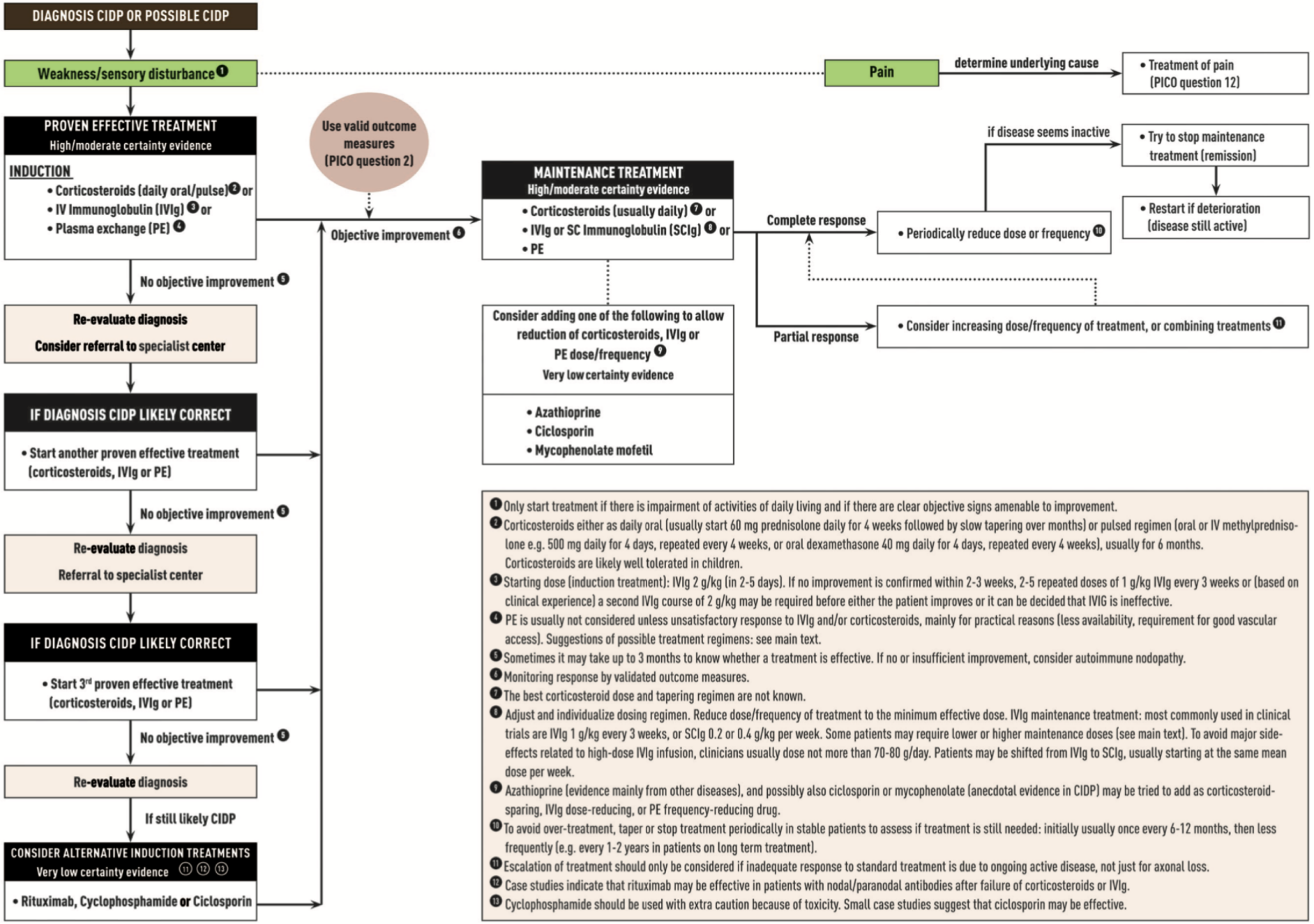

❶ Only start treatment if there is impairment of activities of daily living and if there are clear objective signs amenable to improvement.
❷ Corticosteroids either as daily oral (usually start 60 mg prednisolone daily for 4 weeks followed by slow tapering over months) or pulsed regimen (oral or IV methylprednisolone e.g. 500 mg daily for 4 days, repeated every 4 weeks, or oral dexamethasone 40 mg daily for 4 days, repeated every 4 weeks), usually for 6 months. Corticosteroids are likely well tolerated in children.
❸ Starting dose (induction treatment): IVIg 2 g/kg (in 2-5 days). If no improvement is confirmed within 2-3 weeks, 2-5 repeated doses of 1 g/kg IVIg every 3 weeks or (based on clinical experience) a second IVIg course of 2 g/kg may be required before either the patient improves or it can be decided that IVIG is ineffective.
❹ PE is usually not considered unless unsatisfactory response to IVIg and/or corticosteroids, mainly for practical reasons (less availability, requirement for good vascular access). Suggestions of possible treatment regimens: see main text.
❺ Sometimes it may take up to 3 months to know whether a treatment is effective. If no or insufficient improvement, consider autoimmune nodopathy.
❻ Monitoring response by validated outcome measures.
❼ The best corticosteroid dose and tapering regimen are not known.
❽ Adjust and individualize dosing regimen. Reduce dose/frequency of treatment to the minimum effective dose. IVIg maintenance treatment: most commonly used in clinical trials are IVIg 1 g/kg every 3 weeks, or SCIg 0.2 or 0.4 g/kg per week. Some patients may require lower or higher maintenance doses (see main text). To avoid major side-effects related to high-dose IVIg infusion, clinicians usually dose not more than 70-80 g/day. Patients may be shifted from IVIg to SCIg, usually starting at the same mean dose per week.
❾ Azathioprine (evidence mainly from other diseases), and possibly also ciclosporin or mycophenolate (anecdotal evidence in CIDP) may be tried to add as corticosteroid-sparing, IVIg dose-reducing, or PE frequency-reducing drug.
❿ To avoid over-treatment, taper or stop treatment periodically in stable patients to assess if treatment is still needed: initially usually once every 6-12 months, then less frequently (e.g. every 1-2 years in patients on long term treatment).
⓫ Escalation of treatment should only be considered if inadequate response to standard treatment is due to ongoing active disease, not just for axonal loss.
⓬ Case studies indicate that rituximab may be effective in patients with nodal/paranodal antibodies after failure of corticosteroids or IVIg.
⓭ Cyclophosphamide should be used with extra caution because of toxicity. Small case studies suggest that ciclosporin may be effective.

FLOWCHART 3 Induction and maintenance treatment of CIDP (PICO 8-11)

Sources

- EFNS guideline
- Prairie IVIG Guidelines
- Up to Date
- Neurology Continuum
- Journal articles as cited in presentation

Thank you!

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