CIDP – Life After Diagnosis

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What You Need to Know

- There are treatments!
- There is no “cure”
- A number of things may need to be managed:
  - Your immune system
  - Your pain
  - Your expectations/activity
  - Your independence
  - Your mood
  - Your relationships
  - Your healthcare team

Step #1 is Making Sure Dx is Correct

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Current practice patterns in CIDP: A cross-sectional survey of neurologists in the United States

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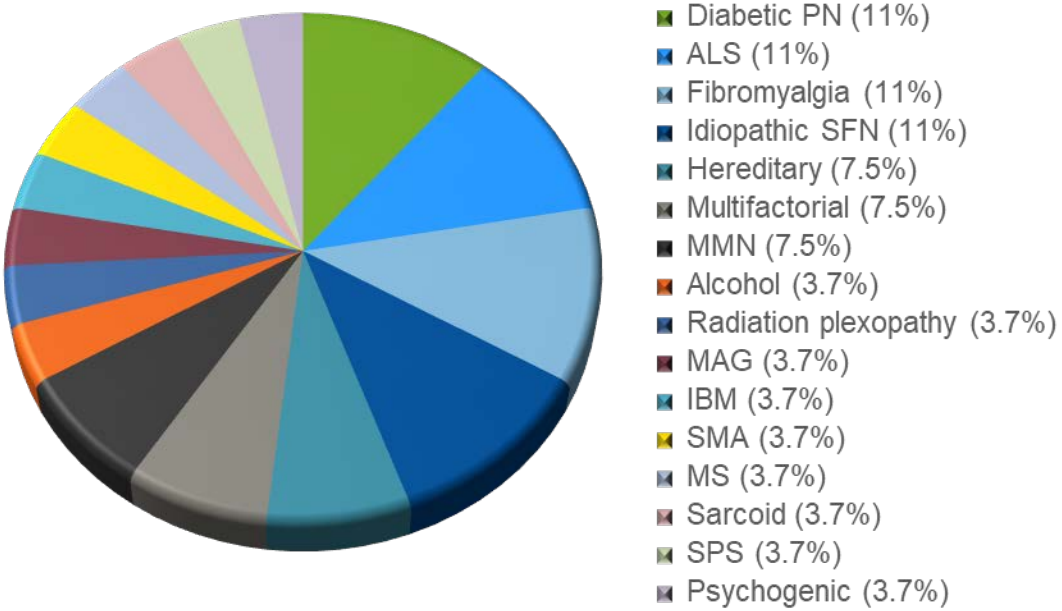
ABSTRACT

To evaluate how neurologists make decisions regarding chronic inflammatory demyelinating polyneuropathy (CIDP), we conducted a cross-sectional quantitative survey of 100 community neurologists in the United States. Only 13% cited using the European Federation of Neurological Societies/Peripheral Nerve Society guideline. In addition, variability in treatment approaches existed regarding the dose of IVIg used, the length of IVIg therapy before determining response, the outcome measures used to determine IVIg response, and the protocol for weaning off therapy. Forty-three percent reported giving doses that were lower than the recommended IVIg loading dose for CIDP. Many reported giving nonspecific patient education about the rationale of IVIg use and treatment duration. The finding that approximately half of community neurologists endorsed electrodiagnostic criteria that do not support CIDP diagnosis indicated difficulties relying heavily upon neurophysiologic studies in diagnostic guidelines. More education on CIDP diagnosis and treatment and a clear, actionable, clinically focused guideline would enhance best practices, particularly in the midst of high information flow and multiple guidelines.

High Rate of CIDP Misdiagnosis

- Retrospective data review for 59 patients referred for second opinion of CIDP
- Patients reclassified 2 separate experts with diagnostic agreement on 58/59 cases
- **CIDP confirmed in 31/58 (53%): Almost half (47%)** of consecutive CIDP referrals (n=58) had an alternative diagnosis

68% with CIDP were managed by neuromuscular specialist vs 37% without CIDP (*P*=0.034)



Reference: Allen JA , Lewis RA. *Neurology.* 2015;85(6):498-504.

Diagnostic Data in CIDP and Not-CIDP Groups

Patients Who Met EFNS/PNS Diagnostic Requirements for CIDP

	Clinical	NCS	CSF	MRI	Biopsy	Improve with Tx
CIDP group (N= 31)	100%	100%	90.3%	75%	50%	89.6%
Not CIDP group (N=27)	44%	14.8%	50%	10.5%	0%	85.7%

- Objective evidence consistent with CIDP seen in a minority of not-CIDP group and yet most felt treatment helped
- Improvement was based on subjective report by patient, not by objective measures

EFNS, European Federation of Neurological Societies; PNS, Peripheral Nerve Society.

Reference: Allen JA , Lewis RA. *Neurology.* 2015;85(6):498-504.

What Caused Misdiagnosis?

- Electrodiagnosis
  - Misinterpreting conduction slowing when CMAP amplitude is reduced
  - Considering slowing at entrapment sites as CIDP
  - Accepting conduction slowing in diabetics as CIDP
- Laboratory
  - Emphasizing mild increases in CSF protein

EFNS, European Federation of Neurological Societies; GBS, Guillain-Barré syndrome; PNS, Peripheral Nerve Society.

Reference: Allen JA , Lewis RA. *Neurology.* 2015;85(6):498-504.

What is Typical CIDP?

A spectrum of conditions with:

- Sensory and motor symptoms
- Distal sensory loss, proximal and distal weakness, and areflexia occurring for more than 2 months
- Demyelination on nerve conduction studies.
- Elevated CSF protein without increase in cell count.
- Normal routine lab studies including protein electropheresis.
- Nerve biopsy showing T cell infiltration and macrophage-associated demyelination.
- Clear response to treatment(s).

There is no gold standard test.

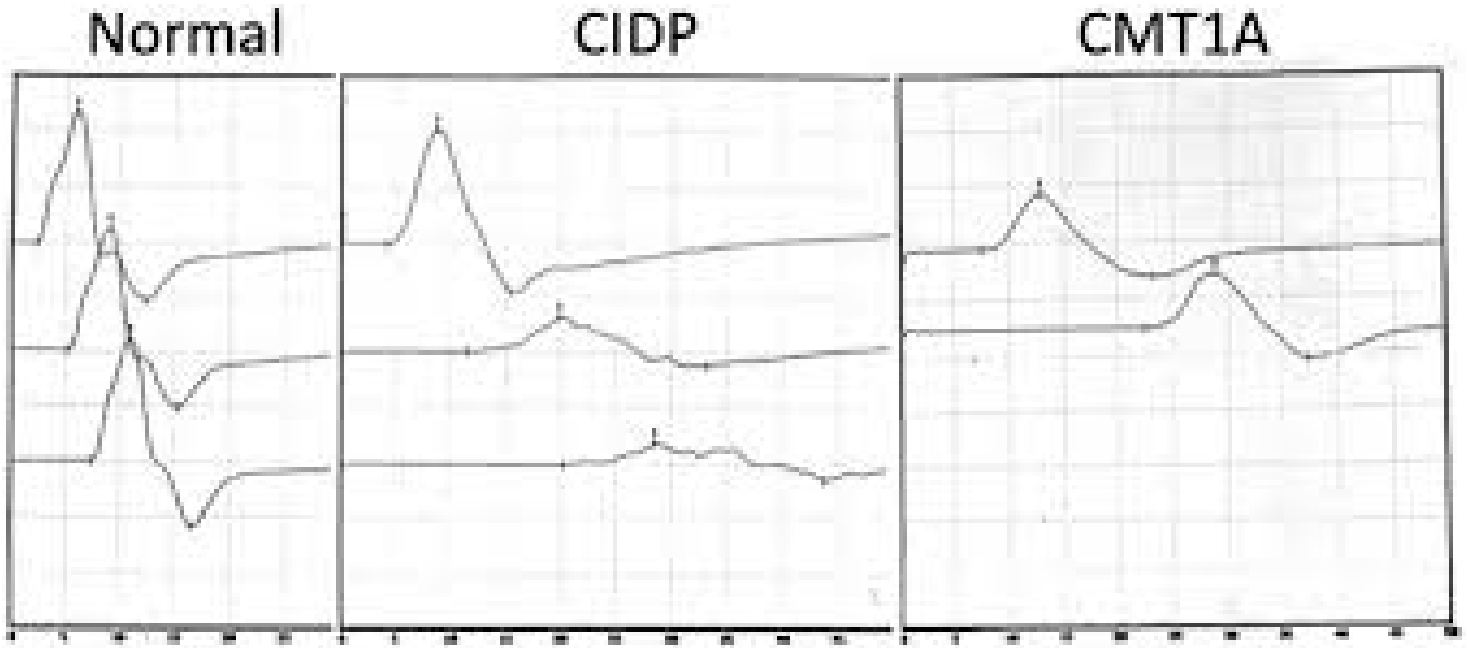
Making the Diagnosis of CIDP

- Careful history with special attention to family history
- Clinical exam with quantitative data
- Tests:
  - NCS/EMG
  - CBC, CMP, B12, and tests for diabetes
  - Protein electrophoresis studies
  - Spinal fluid exam
  - If needed, nerve biopsy

CIDP mimics

- Diabetic neuropathy
- Genetic neuropathy (Charcot-Marie-Tooth disease, CMT)
- Toxic neuropathy
- Lumbar radiculopathy
- Incorrectly performed or interpreted nerve conduction studies

Nerve Conduction Studies



First Line CIDP Treatments

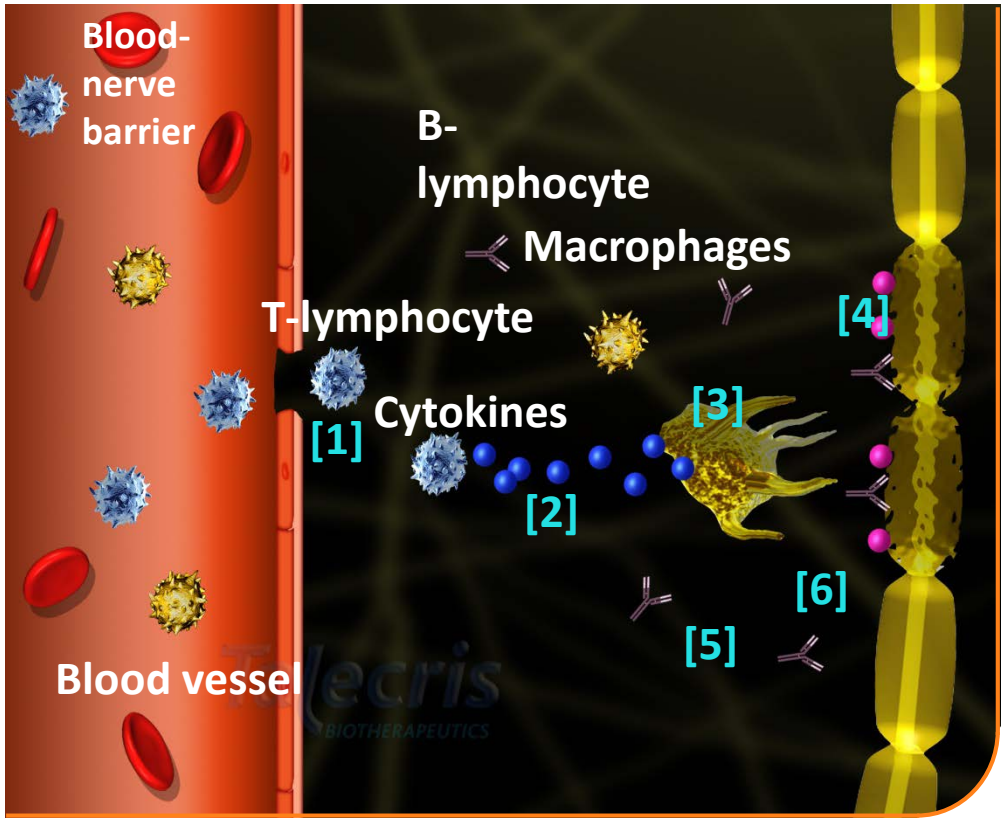
1. Corticosteroids
2. IVIg
3. Plasma exchange

- All three induce significant **short-term** improvements in CIDP.
- Beyond these, evidence for benefit is lacking from randomised clinical trials but many other immunosuppressants are used.

IVIg

- Per ICE trial and the now FDA-approved IVIg regimen, induction of 2 gm/kg over 2-5 days followed by maintenance doses of 1 gm/kg every 3 weeks (over 1-2 days).
- 3 treatments are enough to see if a patient will respond to IVIg.
- Very often, IVIg may be the only treatment needed.
- Not everyone with CIDP will respond to IVIg

Possible Mechanism of Immune Modulation by IVIG in CIDP



Possible mechanism*

[1] Modulation of adhesion molecules

[2] Modulation of inflammatory and anti-inflammatory cytokines

[3] Modulation of Fc receptors on macrophages

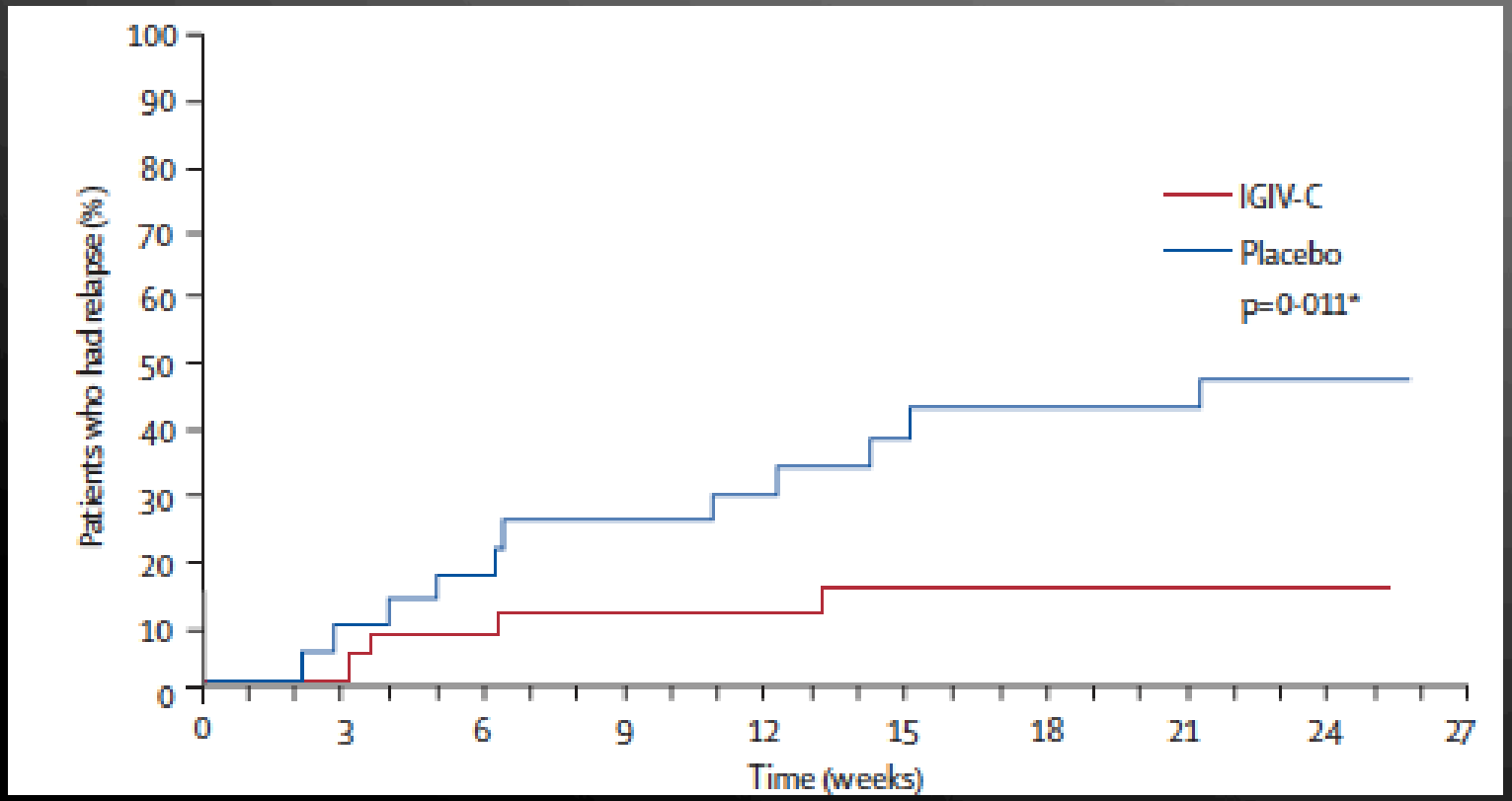
[4] Complement inhibition

[5] Influence on production and degradation rate of pathogenic autoantibodies

[6] Neutralization of anti-idiotypic antibodies

*Dalakas MC. *Neurology.* 2002; [illegible] suppl 6):S13-S21.

Time to Relapse



IVIg Infusions

- If you are having problems, review the following:
  - Are you being hydrated before and after?
  - Is your rate slow at first and then increased slowly?
  - Are you being pre-medicated especially for headache?
  - Was your brand changed?

BCPT
Basic & Clinical Pharmacology & Toxicology

Basic & Clinical Pharmacology & Toxicology, 2015, **117**, 409–412 Doi: 10.1111/bcpt.12428

Headache and Nausea after Treatment with High-Dose Subcutaneous *versus* Intravenous Immunoglobulin

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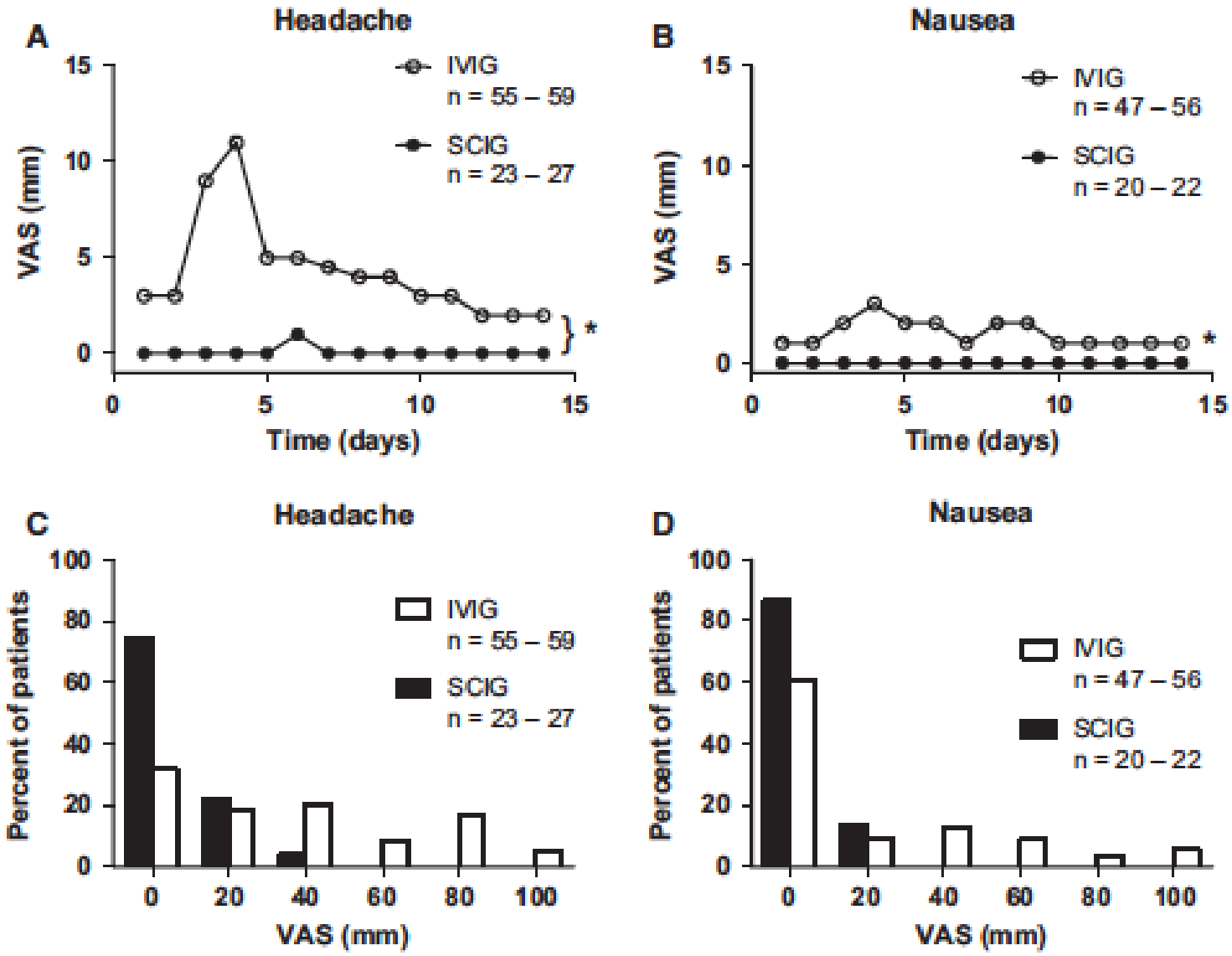
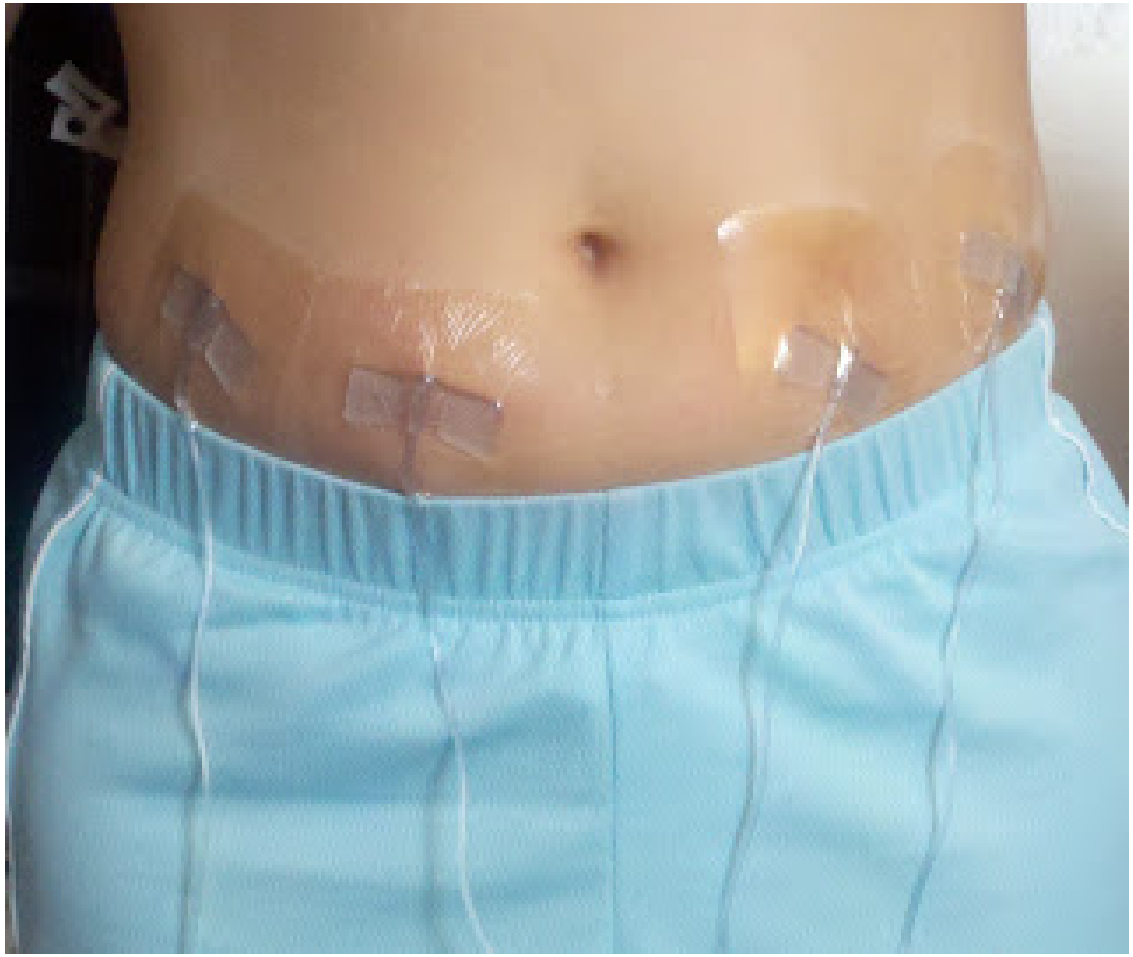

A
Headache
VAS (mm)
Time (days)
IVIG
n = 55 – 59
SCIG
n = 23 – 27
*
B
Nausea
VAS (mm)
Time (days)
IVIG
n = 47 – 56
SCIG
n = 20 – 22
*
C
Headache
Percent of patients
VAS (mm)
IVIG
n = 55 – 59
SCIG
n = 23 – 27
D
Nausea
Percent of patients
VAS (mm)
IVIG
n = 47 – 56
SCIG
n = 20 – 22

Subcutaneous Immunoglobulin (SCIG)

- Administered through needles in the skin instead of intravenous
- Initially used for immunodeficiency disorders
- Recently FDA approved for CIDP



Potential Reasons to Switch to SCIG

- IV access issues
- Side effects
- Wear off
- Patient logistics/autonomy
- IVIG risk factors?

Potential Problems with Switching to SCIG

- Figuring out dose
- Figuring out sites and rates of infusion

- It is important to work with someone knowledgeable about administering this treatment

Corticosteroids

- Traditionally, prednisone at high dose (40-60 mg per day).
- Can have many side effects
  - Weight gain
  - Insomnia
  - Diabetes
  - Hypertension
  - Depression
  - Irritability
  - Cataracts
  - Stomach ulcers

Other Corticosteroid Options

- “Pulse” treatment
  - large dose given occasionally
- Methylprednisolone (Solumedrol)
  - Intravenous, weekly or monthly
  - Less than 30 minutes per dose
  - Can be done at home
- Dexamethasone (Decadron)
  - 5 pills per (40 mg) day for 4 days each month

Common reasons to change treatment

1. No therapeutic response.
2. Some therapeutic response, but trying to do better.
3. Side effects.
4. Responded reasonably, but unable to wean.

Trouble Shooting

- If sub-optimal response
  - This can be hard as response may take a **long** time to become "optimal."
  - Try another first-line agent before considering combinations.
  - Special circumstances may dictate other treatments.
- If no response
  - Consider alternative diagnoses.
  - Try a different first-line treatment.
- Adverse events
  - Tweak something.
  - Try another first-line treatment.

Other agents in CIDP

Long list of immunosuppressants

- Mycophenolate mofetil (CellCept)
- Azathioprine (Immuran)
- Cytoxan
- Rituximab

Outcome Measures

- Ideally, should be clinically meaningful improvement in daily activities.
- Subject measurement scales – RODS
- Exam scales – NIS, MRC sumscore
- Measurement tools – Martin Vigoromete Jamar grip meter, Rydel Seiffer tuning fork, monofilaments (how many of you have ever seen these).

NEUROLOGY

Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies

S.I. van Nes, E.K. Vanhoutte, P.A. van Doorn, et al.

Neurology 2011;76:337

Are you able to	Task	Not possible to perform [0]	Possible, but with some difficulty [1]	Possible, without any difficulty [2]
1.	read a newspaper/book?	☐	☐	☐
2.	eat?	☐	☐	☐
3.	brush your teeth?	☐	☐	☐
4.	wash upper body?	☐	☐	☐
5.	sit on a toilet?	☐	☐	☐
6.	make a sandwich?	☐	☐	☐
7.	dress upper body?	☐	☐	☐
8.	wash lower body?	☐	☐	☐
9.	move a chair?	☐	☐	☐
10.	turn a key in a lock?	☐	☐	☐
11.	go to the general practitioner?	☐	☐	☐
12.	take a shower?	☐	☐	☐
13.	do the dishes?	☐	☐	☐
14.	do the shopping?	☐	☐	☐
15.	catch an object (e.g., ball)?	☐	☐	☐
16.	bend and pick up an object?	☐	☐	☐
17.	walk one flight of stairs?	☐	☐	☐
18.	travel by public transportation?	☐	☐	☐
19.	walk and avoid obstacles?	☐	☐	☐
20.	walk outdoor < 1 km?	☐	☐	☐
21.	carry and put down a heavy object?	☐	☐	☐
22.	dance?	☐	☐	☐
23.	stand for hours?	☐	☐	☐
24.	run?	☐	☐	☐

Mark the best option with "x"

Obtain Another Opinion From a Center of Excellence if…

- You do not have the typical features of CIDP but are receiving treatment(s) for CIDP.
- CIDP was diagnosed mainly based on nerve conduction studies or spinal fluid protein.
- You are not clearly improving on your current treatment(s).
- You have been on treatment(s) for a long time and are stable.