the FOUNDATION for PERIPHERAL NEUROPATHY®

Welcome!

FPN Webinar:

PN Myths vs. Facts: Deepening Understanding & Raising Awareness

Thursday, May 8, 2025

We will begin our presentation shortly.

the FOUNDATION *for* PERIPHERAL NEUROPATHY®

Today's moderator:

Lindsay Colbert
Executive Director
the Foundation *for* Peripheral Neuropathy

Before We Begin

This presentation is being recorded. The recording link will be emailed to you so you can view it again later.

Submit your questions anytime via the Questions Box. We will try to answer them during this webinar.

We are now pleased to offer closed captioning. Check your dashboard to activate the tool.

the FOUNDATION for PERIPHERAL NEUROPATHY®

Today's Expert:

Shanna Patterson, MD, MS
Site Chair, Department of Neurology, Mount Sinai West Side Operations
Director for Special Projects in System-wide Neurology Clinical Operations
Associate Professor, Department of Neurology

Peripheral Neuropathy Myths vs. Facts

Deepening Understanding and Raising Awareness

Shanna K. Patterson, MD, MS

May 2025

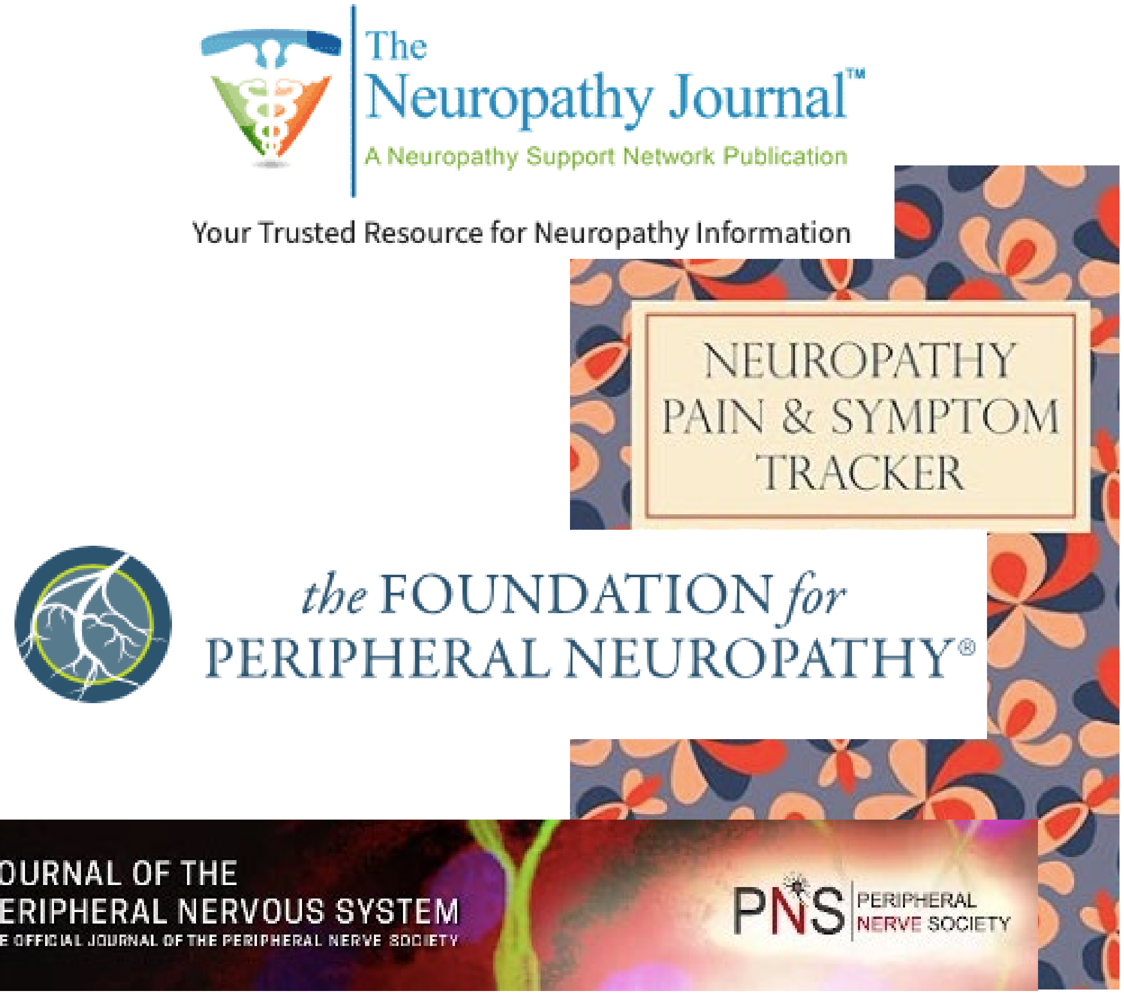
Neuropathy

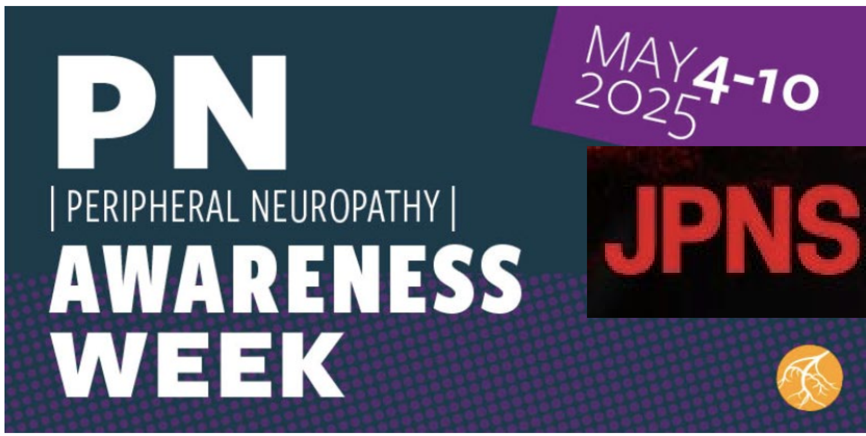
One of the most prevalent neurologic conditions encountered by physicians of all specialties

Prevalence:

2.4% in the general population

8% over age 55





Mayo Clin Proc. 2015;90(7):940-951

https://www.amazon.com/Neuropathy-Pain-Symptom-Tracker-Management/dp/B097SRZGSB

Myth #1
Peripheral Neuropathy is a Modern Disease

Historical Perspectives, Human Contexts – Nerve Pain

- Origins of the word pain, from the Greek *Poin* (*punishment*)
- Aristotle considered the *heart* as the origin of pain
- Galen declared the *brain* was the organ involved in pain perception and transmission was through *invisible* nerves
- Nerve originated pain first described during medieval period
- Robert Graves observing patients in 1828 pointed out:
  "the disease may be resident in the **nervous cords themselves**"

Galen (130-200 CE)
Roman and Greek Physician, Surgeon and Philosopher

Graves (1796-1853)
Irish surgeon

Acta Med Hist Adriat 2015:13 Suppl 2:9-22.
Arch NeurPsych. 1934;32(2):377-394
https://en.wikipedia.org/wiki/Galen
https://www.eurothyroid.com/about/met/graves.html

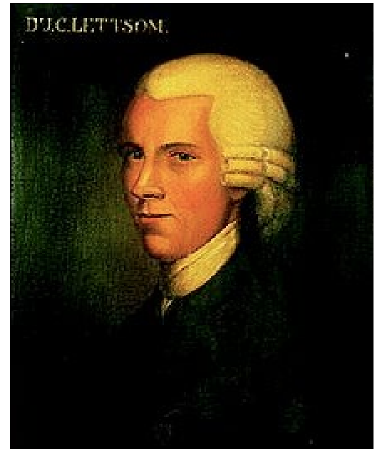
Historical Perspectives, Clinical Contexts – Peripheral "Neuritis"

Freeman, W. Peripheral Neuritis. [*Med. Ann., District of Columbia,* 3: No. 7, July, 1934.]

Peripheral neuritis occurs in such diverse affections as leprosy and lead poisoning and Landry's paralysis. It may be confined to the terminal filaments of a single nerve or may involve practically every nerve in the body; it may pass off without residuals or it may kill the patient or leave him permanently crippled. The etiology is extremely variable. Most emphasis is laid in this paper upon the toxic or deficiency polyneuritides and upon the treatment. (Author's abstract.)

Viets, H. R. History of Peripheral Neuritis as a Clinical Entity. [*Arch. Neurol. & Psychiat.,* 32: 377.]

Early descriptions of peripheral neuritis caused by, or associated with, alcoholism or deficiency of food were given by John C. Lettsom in 1787, in London, and James Jackson in 1822, in this country. Subsequently Robert J. Graves, the English clinician, described an epidemic of neuritis which oc-



John C. Lettsom (1744-1815)
English Physician and Philanthropist
Founded the Medical Society of London

Jean B. O. Landry (1866–1940)
French Physician and Researcher
First Described GBS

→ *Different <u>leading causes</u> of neuropathy in different eras, but the clinical condition is the same*

https://en.wikipedia.org/wiki/John_Coakley_Lettsom

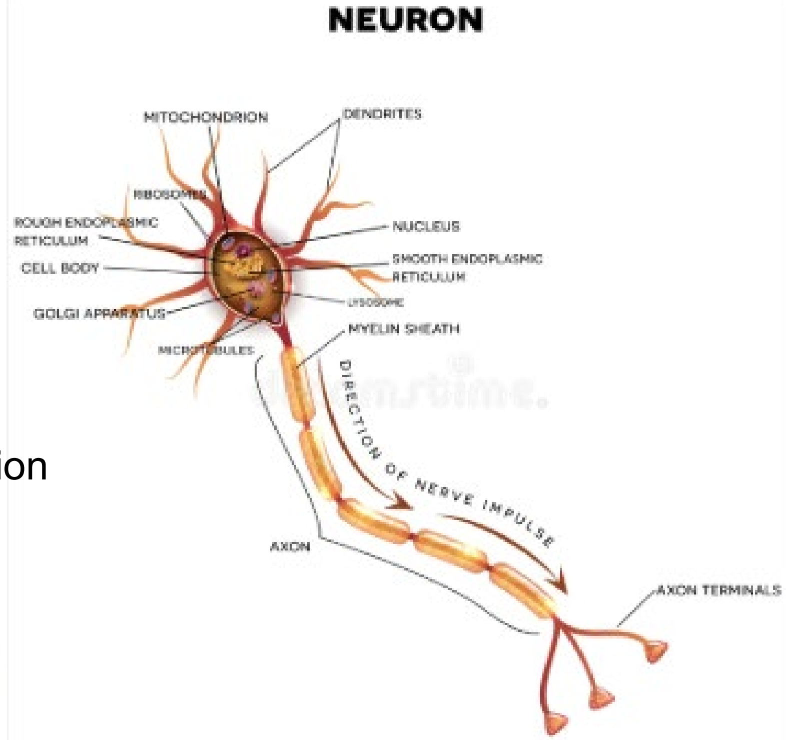
https://litfl.com/jean-baptiste-octave-landry/

Myth #2

Peripheral Neuropathy is a Single Disease

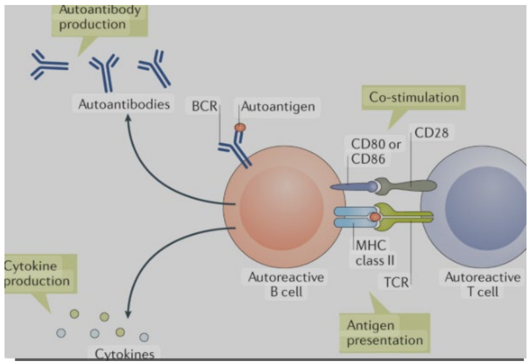
Many different underlying types of nerve insults contribute to different types of PN, resulting in different clinical presentations and disease courses…

Hereditary



Blood Vessel Inflammation

Autoimmune



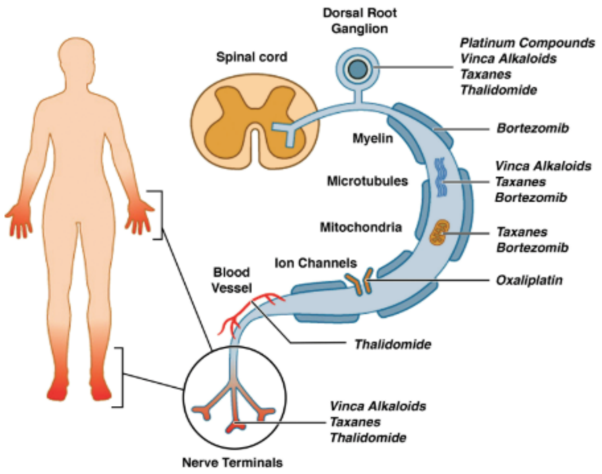
Dreamstime.com

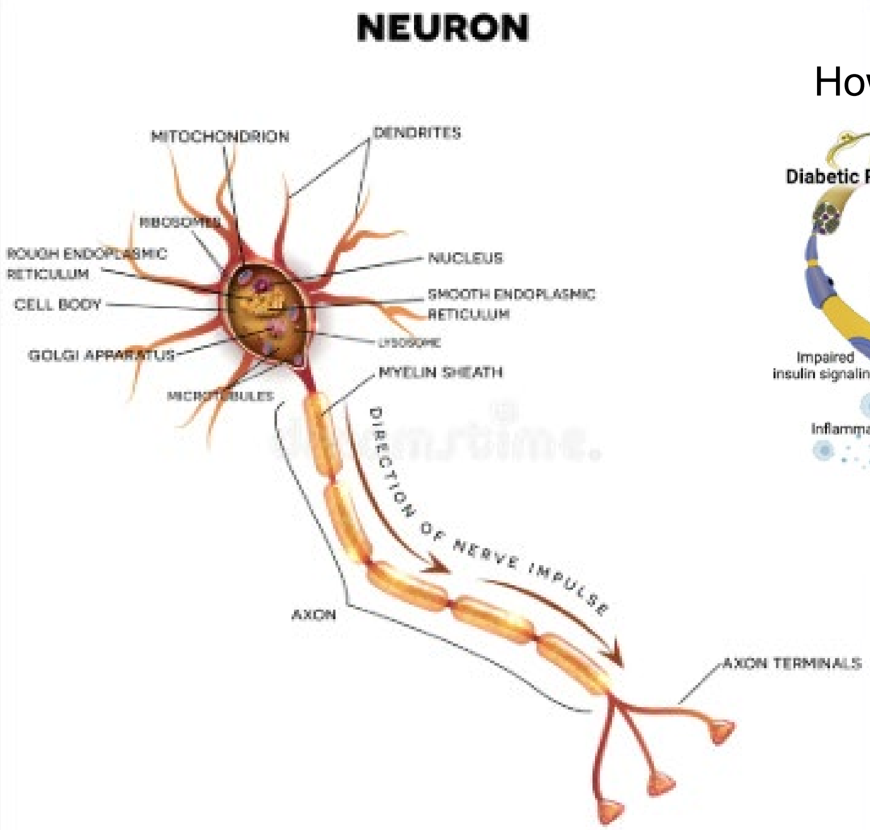
https://www.nature.com/articles/s41584-019-0211-0

https://www.linkedin.com/pulse/understanding-diabetic-peripheral-neuropathy-risk-rajaratnam-o0yyc

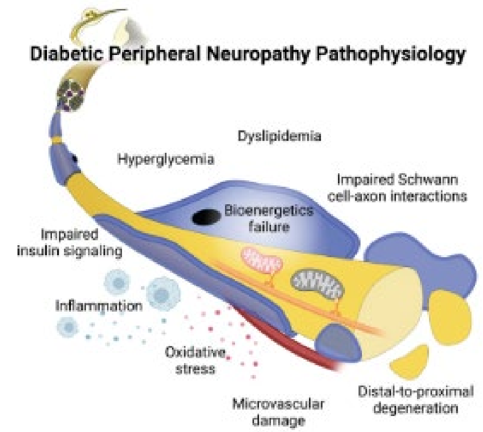
https://science.howstuffworks.com/life/cellular-microscopic/dna.htm

How chemotherapy causes PN





How diabetes causes PN



Because the mechanisms for neuropathy are so varied, it makes sense that there might not be a one-size-fits-all peripheral neuropathy treatment or cure, but rather different strategies for different causes

https://journals.sagepub.com/doi/10.1177/0192623319861937
https://www.nature.com/articles/s41584-019-0211-0

Myth #3

Our Understanding of Neuropathy has Stalled, Especially when it comes to ***Idiopathic Neuropathy***

Causes of Neuropathy

- Neuropathy cause identified in majority of cases
- *Idiopathic* diagnosis for <u>25% to 46% of cases</u>

Mayo Clin Proc. 2015;90(7):940-951
Am Fam Physician 2020;102(12):732-739

Idiopathic Neuropathy: What are we Missing?

Are we missing things we can't test for? (medication/environmental toxicities/prior exposure/prior infection)

Are we missing things we can't test for *yet*? (hereditary, complex immune)

OR....

Is there something <u>relatively common</u> causing neuropathy that may be challenging to prove on an individual level

Metabolic Syndrome and Neuropathy

Published in final edited form as:
J Neurol Sci. 2008 October 15; 273(1-2): 25–28. doi:10.1016/j.jns.2008.06.005.

Idiopathic Neuropathy Patients are at High Risk for Metabolic Syndrome

A. Gordon Smith, MD[1,2], **Kristi Rose, MD**[3], and **J. Robinson Singleton, MD**[1]

1*University of Utah Department of Neurology*

2*University of Utah Department of Pathology*

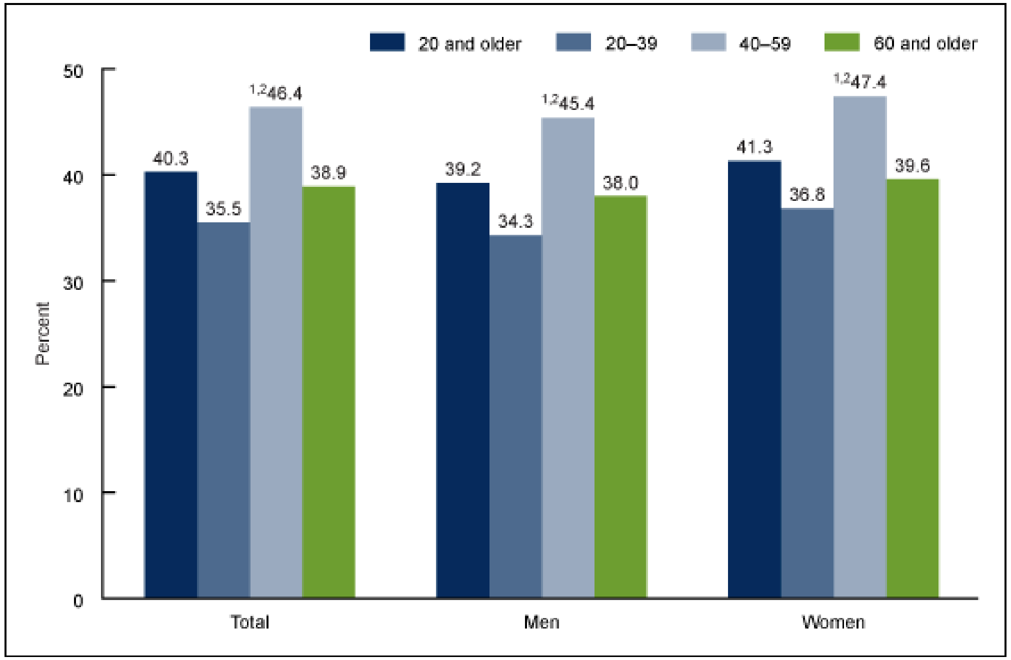
3*University of Utah School of Medicine*

Results—Contrary to our hypothesis, neuropathy patients with normoglycemia and IGT shared a similarly elevated prevalence of metabolic syndrome features compared to published normal populations. Compared to diabetic subjects without neuropathy, the normoglycemic neuropathy patients had significantly higher total and LDL cholesterol, and a higher prevalence of abnormal HDL and triglycerides. The prevalence of obesity and hypertension were similar among patient groups. Normoglycemic neuropathy subjects had significantly more features of metabolic syndrome (other than hyperglycemia) than diabetics.

Metabolic Syndrome and Neuropathy

- **Metabolic Syndrome**, WHO (1999)
  - Impaired glucose tolerance, diabetes and/or insulin resistance + 2 or more of the following:
    - High BP
    - Elevated triglycerides (or on treatment)
    - Low HDL
    - Central obesity
    - Microalbuminuria
  - *Abdominal fat cells raise levels of free fatty acids, which contribute to insulin resistance, inflammation*

Figure 1. Prevalence of obesity in adults age 20 and older, by sex and age: United States, August 2021–August 2023



https://www.cdc.gov/obesity/adult-obesity-facts/index.html

Metabolic Syndrome and Neuropathy

Studies have shown a higher risk of neuropathy in the setting of obesity, even in the absence of diabetes or pre-diabetes.

Original Investigation

December 2016

Association Between Metabolic Syndrome Components and Polyneuropathy in an Obese Population

Brian C. Callaghan, MD, MS[1]; Rong Xia, MS[2]; Evan Reynolds, MS[2]; et al

» Author Affiliations | Article Information

JAMA Neurol. 2016;73(12):1468-1476. doi:10.1001/jamaneurol.2016.3745

Polyneuropathy Prevalence Stratified by Glycemic Status

The prevalence of polyneuropathy was 3.8% (2 of 53) in the lean control group, 11.1% (5 of 45) in the obese participants with normoglycemia, 29% (9 of 31) in the obese participants with prediabetes, and 34.6% (9 of 26) in the obese participants with diabetes (*P*<.01 for trend).

In obese and lean control populations who received comprehensive metabolic and neuropathy phenotyping, we found a higher prevalence of neuropathy in obese patients with normoglycemia compared with lean controls. The prevalence of neuropathy continued to increase in obese patients with prediabetes and diabetes. Diabetes, waist circumference, and likely prediabetes were the main metabolic factors associated with neuropathy. In contrast, systolic blood pressure, triglyceride levels, and HDL cholesterol levels were not associated with neuropathy. Future intervention studies are needed to confirm a causal association between these metabolic factors and neuropathy.

Received: 22 June 2020 | Revised: 2 September 2020 | Accepted: 4 October 2020
DOI: 10.1002/mus.27086

INVITED REVIEW

Answer questions and earn CME https://education.aanem.org/URL/JR80.

MUSCLE&NERVE WILEY

Metabolic syndrome and peripheral neuropathy

Mohamed Kazamel MD[1] | Amro Maher Stino MD[2] | Albert Gordon Smith MD[3]

CI, 1.15-1.75) were significantly associated with DSP. In addition, waist circumference was significantly associated with multiple secondary neuropathy outcomes, including the presence of any neuropathic symptoms (OR, 1.07; 95% CI, 1.03-1.11), the inability to feel heavy monofilament (OR, 1.10; 95% CI, 1.03-1.17), peroneal compound muscle action potential amplitude (OR, −0.05; 95% CI, −0.09 to −0.01), and vibration detection threshold (OR, 0.58; 95% CI, 0.01-1.14), independent of glycemic status. Low HDL was significantly associated with a few secondary outcomes, including the presence of any neuropathic symptoms (OR, 0.091; 95% CI, 0.85-0.97) and the inability to feel light monofilament (OR, 0.92; 95% CI, 0.86-0.98). All associations were independent of glycemic status.[42] A Dutch study similarly found CSPN to be more prevalent as more components of MetS were fulfilled. The association with CSPN was particularly strong for waist circumference and hypertriglyceridemia and was independent of glycemic status.[43] A longitudinal German study also showed general and abdominal obesity to be associated with the development of CSPN.[44]

4.2 | CSPN is associated with dyslipidemia

Elevated triglycerides and reduced HDL are components of MetS. Robust literature links hypertriglyceridemia to the development of CSPN. Hughes et al reported significantly higher triglyceride levels in CSPN when compared with healthy control patients, with triglyceride levels being higher in patients with painful CSPN.[45] In a separate longitudinal study, hypertriglyceridemia was associated with reduced sural nerve myelin fiber density in DPN patients.[46] Hyper-

Myth #4
There are no New Treatments for Neuropathy

New Treatment for Autoimmune Neuropathy:
First new CIDP Treatment in 30 Years Approved in 2024

FDA approves treatment for chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

June 2024

Action

The U.S. Food and Drug Administration has approved Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults. Vyvgart Hytrulo is a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase. Vyvgart Hytrulo was previously approved for the treatment of adults with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.

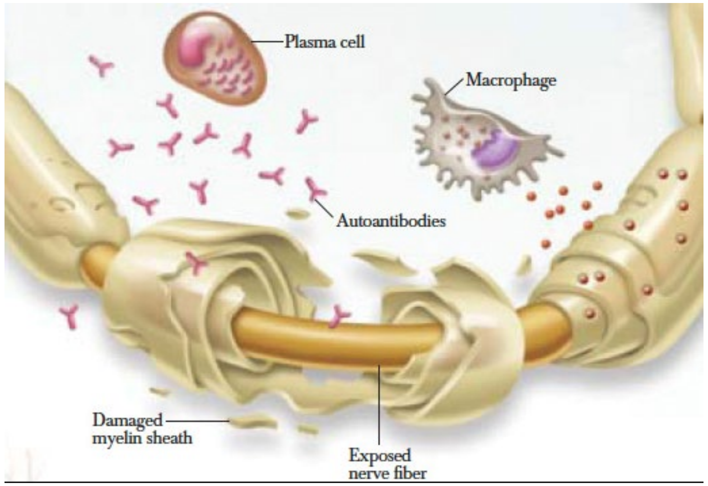
For CIDP, Vyvgart Hytrulo is administered subcutaneously (under the skin) as weekly injections. The recommended dose is detailed in the prescribing information.

https://www.vyvgart.com/

Argenx.com

New Treatment for Autoimmune Neuropathy:
First new CIDP Treatment in 30 Years Approved in 2024

CIDP Nerve Damage



The first major innovation in CIDP treatment in over 30 years*

The complete cause of chronic inflammatory demyelinating polyneuropathy (CIDP) is not fully understood. Recent studies suggest that in some people, harmful antibodies like the harmful IgG, may be involved in damaging myelin. VYVGART Hytrulo is specifically designed to cause a reduction in the number of IgG antibodies, including harmful IgG antibodies.

*VYVGART Hytrulo contains efgartigimod alfa and hyaluronidase, and is specifically designed to attach to FcRn receptors.
FcRn=neonatal Fc receptor; IgG=immunoglobulin G

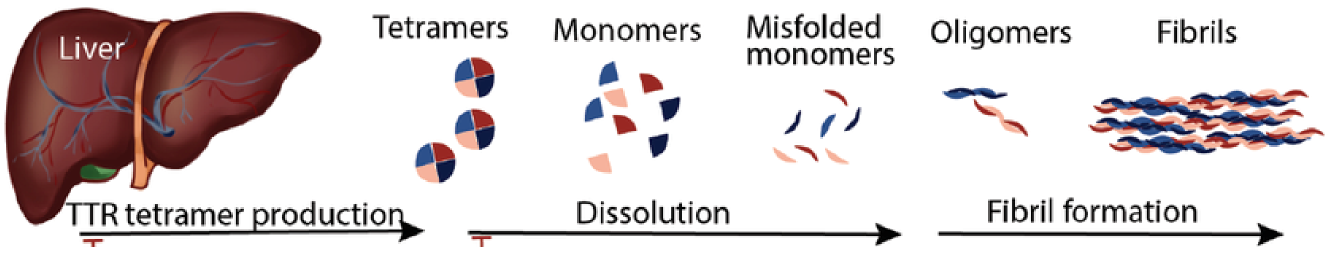
Fc receptor blockers, such as efgartigimod, lead to a reduction in circulating IgG levels and a decrease in IgG-mediated immune responses, potentially alleviating conditions where IgG autoantibodies contribute to illness.

https://www.vyvgart.com/

Argenx.com

https://www.physio-pedia.com/Chronic_Inflammatory_Demyelinating_Polyneuropathy_%28CIDP%29

New Treatment for Hereditary Neuropathy:
Transthyretin (TTR) Neuropathy



TTR neuropathy is caused by the buildup of misfolded TTR proteins in the body, primarily in the peripheral nervous system. These misfolded proteins form amyloid fibrils, which deposit in nerves, causing damage and leading to neuropathy.

https://practicalneurology.com/

New Treatment for Hereditary Neuropathy: Transthyretin (TTR) Neuropathy

> Neurol Ther. 2023 Oct;12(5):1759-1775. doi: 10.1007/s40120-023-00522-4. Epub 2023 Jul 31.

Impact of Vutrisiran on Quality of Life and Physical Function in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy

Laura Obici [1], Senda Ajroud-Driss [2], Kon-Ping Lin [3], John L Berk [4], Julian D Gillmore [5], Parag Kale [6], Haruki Koike [7], David Danese [8], Emre Aldinc [8], Chongshu Chen [8], John Vest [8], David Adams [9]; HELIOS-A Collaborators Study Group

Collaborators, Affiliations + expand

PMID: 37523143 PMCID: PMC10444729 DOI: 10.1007/s40120-023-00522-4

Conclusion: Vutrisiran treatment provided significant clinical benefits in multiple measures of QOL and physical function in patients with ATTRv amyloidosis with polyneuropathy. Benefits were most pronounced in patients with earlier-stage disease, highlighting the importance of early diagnosis and treatment.

Trial registration number: ClinicalTrials.gov: NCT03759379.

Randomized Controlled Trial > Amyloid. 2023 Mar;30(1):1-9.
doi: 10.1080/13506129.2022.2091985. Epub 2022 Jul 23.

Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial

David Adams [1], Ivailo L Tournev [2 3], Mark S Taylor [4], Teresa Coelho [5], Violaine Planté-Bordeneuve [6], John L Berk [7], Alejandra González-Duarte [8], Julian D Gillmore [9], Soon-Chai Low [10], Yoshiki Sekijima [11], Laura Obici [12], Chongshu Chen [13], Prajakta Badri [13], Seth M Arum [13], John Vest [13], Michael Polydefkis [14]; HELIOS-A Collaborators

Collaborators, Affiliations + expand

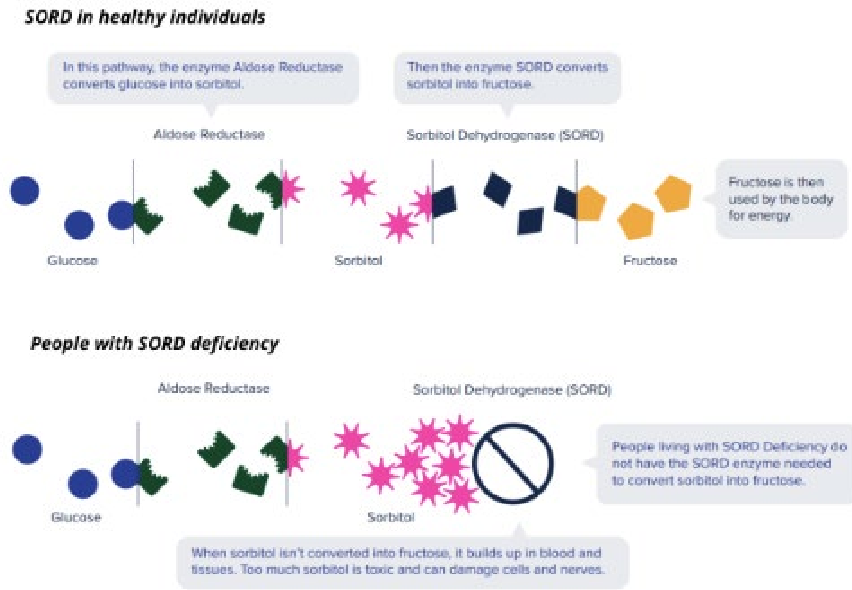
PMID: 35875890 DOI: 10.1080/13506129.2022.2091985

Free article

Abstract

Background: The study objective was to assess the effect of vutrisiran, an RNA interference therapeutic that reduces transthyretin (TTR) production, in patients with hereditary transthyretin (ATTRv) amyloidosis with polyneuropathy.

Treatments on the Horizon for Hereditary Neuropathy:
CMT-Sorbitol Dehydrogenase Deficiency



WHAT IS CMT-SORD?

CMT-SORD, also known as Sorbitol Dehydrogenase Deficiency, is a recently discovered, unique type of Charcot-Marie-Tooth disease (CMT). Identified in May 2020 with funding from CMTA, this type of CMT is caused by mutations in the SORD gene. These mutations lead to the buildup of a sugar alcohol called sorbitol, which becomes toxic to the nerves as it accumulates in the body. This toxicity results in CMT-SORD symptoms, including muscle weakness and sensory loss.

https://www.cmtausa.org/understanding-cmt/types-of-cmt/sord/

https://cmtrf.org/a-new-trial-for-cmt/

Treatments on the Horizon for Hereditary Neuropathy:
CMT-Sorbitol Dehydrogenase Deficiency

Functional Improvement Seen With Govorestat in SORD Deficiency Trial

MPR MEDICAL PROFESSIONALS REFERENCE Diana Ernst, RPh | February 16, 2024

The phase 3 double-blind, placebo-controlled INSPIRE trial (ClinicalTrials.gov: NCT05397665) included 56 patients aged 16 to 55 years with genetically-confirmed SORD deficiency (blood sorbitol levels >10,000ng/mL). Study participants were randomly assigned to receive govorestat orally once daily or placebo.

Findings from the 12-month interim analysis showed sustained and significant reductions in sorbitol levels with govorestat compared with placebo (P <.001). This effect significantly correlated with the prespecified Charcot Marie Tooth Functional Outcome Measure (CMT-FOM) composite endpoint (10-meter walk-run test, 4 stair climb, sit to stand test, 6-minute walk test and dorsiflexion; primary endpoint; P =.05). CMT-FOM is a performance-based assessment that measures the functional ability of patients with neuropathies.

Govorestat was also associated with a statistically significant effect on the CMT Health Index, a patient-reported outcome measure, with improvements seen in lower limb function, mobility, fatigue, pain, sensory function, and upper limb function (secondary endpoint; P =.01).

Treatments on the Horizon for Hereditary Neuropathy:
CMT-Sorbitol Dehydrogenase Deficiency

People living with Sorbitol Dehydrogenase (SORD) Deficiency are missing the SORD enzyme required to metabolize sorbitol. High sorbitol levels in blood and tissues cause CMT (Charcot-Marie-Tooth) and HMN (Hereditary Motor Neuropathy) symptoms.

You may qualify to get tested for SORD Deficiency at no cost and find out if you can participate in a new clinical trial in SORD Deficiency. A nurse will visit your home to draw a blood sample — it only takes a few minutes, and you will receive your results within a few weeks.

Eligibility requirements for the blood test include:

- 16–55 years of age
- with a clinical diagnosis of a hereditary neuropathy

Neuropathy Treatments under Investigation:
GLP1 Agonists and Diabetic Neuropathy

GLP1 Agonists:

A relatively new class of medications that help manage blood sugar levels in people with type 2 diabetes, and can also help treat obesity.

Drug
Dulaglutide **(Trulicity)**
Exenatide **(Byetta)**
Exenatide Extended Release **(Bydureon BCise)**
Liraglutide **(Victoza)**
Lixisenatide **(Adlyxin)**
Semaglutide subcutaneous, tablet **(Ozempic, Rybelsus)**
Tirzepatide **(Mounjaro)**

Diabetologia. 2024 Mar;67(3):561-566. doi: 10.1007/s00125-023-06072-6. Epub 2024 Jan 8.

Glucagon-like peptide-1 receptor agonists reverse nerve morphological abnormalities in diabetic peripheral neuropathy

Roshan Dhanapalaratnam [1, 2], Tushar Issar [1], Alexandra T K Lee [3], Ann M Poynten [3], Kerry-Lee Milner [3], Natalie C G Kwai [4], Arun V Krishnan [5, 6]

Affiliations + expand

PMID: 38189936 DOI: 10.1007/s00125-023-06072-6

Methods: Nerve structure was assessed using peripheral nerve ultrasonography and measurement of tibial nerve cross-sectional area, in conjunction with validated neuropathy symptom scores and nerve conduction studies. A total of 22 consecutively recruited participants with type 2 diabetes were assessed before and 1 month after commencing GLP-1 RA therapy (semaglutide or dulaglutide).

Conclusions/interpretation: This study demonstrates the efficacy of GLP-1 RAs in improving neuropathy outcomes, evidenced by improvements in mainly structural and morphological measures and supported by electrophysiological and clinical endpoints. Future studies, incorporating quantitative sensory testing and measurement of intraepidermal nerve fibre density, are needed to investigate the benefits for small fibre function and structure.

https://www.hca.wa.gov/assets/billers-and-providers/antidiabetics-GLP-1-agonists.pdf

Myth #5
There is Nothing I can do to Make a Difference

Advocacy Starts with You… and *for* You!

American Academy of Neurology

Four Key Steps in Advocacy

- **Introduce yourself**
  - Humanize your experience, form a relationship
- **Tell your story**
- **Make the ask**
  - What are your priorities?
    - Treatment for pain, improved mobility
  - Set some goals
    - Timelines
- **Follow-up**

Advocacy

Self-Advocacy Contexts:

Health care team

Patient support groups

Physical therapist

Pharmacist

Advocacy Starts with Us!

Advocacy and Public Policy

The Foundation *for* Peripheral Neuropathy (FPN) works to support public policies that benefit people with peripheral neuropathy. FPN advocates for federal and state legislation as well as regulatory actions that will eventually benefit PN patients and help ensure funding for further research.

Right now we are asking Congress to fully restore CDMRP (Congressionally Directed Medical Research Program) funding to ensure medical research continues. Write to your representative to ask for their support of this critical program.

Our Policy Targets

While priority issues change from year to year, our main focus is increasing federal investment in research at the National Institutes of Health (NIH) and the Department of Defense (DoD), in order to improve the diagnosis, treatment, and management of peripheral neuropathy.

the FOUNDATION *for* PERIPHERAL NEUROPATHY

How to Take Action for More Research for Peripheral Neuropathy

What to do:

Contact the office of your U.S. Senators and ask that they support "Peripheral Neuropathy" as a condition eligible for study through the Department of Defense Peer-Reviewed Medical Research Program (PRMRP) during the Fiscal Year 2026 appropriations process.

How to do it:

- Complete the letter below with your PN story.
- Include your mailing address in your letter to establish that you are a constituent of the state your Senator represents.
- Send the letter by email to your Senators. You can find their emails and other contact information by clicking here.
- Please share your correspondence with us by send a copy of your communication to our government relations consultant, Mark Vieth, at mvieth@dc-crd.com.

Thank You

Mount Sinai

the FOUNDATION for PERIPHERAL NEUROPATHY®

Questions?

the FOUNDATION *for* PERIPHERAL NEUROPATHY®

Thank You for Watching!

Did you like this webinar? Please take our survey at the end of this webinar. A recording will be uploaded on our website at www.foundationforpn.org shortly. Stay tuned.

Do you like us? Please consider supporting us so that we can continue to fulfill our mission of improving the lives of people living with Peripheral Neuropathy. You can give securely online, via mail or via phone. Every dollar matters!

Can we help with anything else? Call 847-883-9942 or email info@tffpn.org. You may also mail inquiries and donations to *the* Foundation *for* Peripheral Neuropathy at 2700 Patriot Blvd, Suite 250, Glenview, Illinois 60026.