Do you have Charcot-Marie-Tooth Type 2 (CMT2) or Distal Hereditary Motor Neuropathy (dHMN) with an unknown genetic cause of disease?

If so, you may have SORD Deficiency.

What is SORD Deficiency?

Sorbitol Dehydrogenase (SORD) Deficiency, also called CMT-SORD or SORD Neuropathy, is a recently discovered rare, progressive, debilitating, genetic disease that affects approximately 1 in 100,000 people.[4] In the United States, it is estimated that there are 3,300 individuals living with the disease.[4]

Before the discovery of the SORD gene in 2020[2], people living with SORD Deficiency were diagnosed based on their symptoms as having CMT2 or dHMN[2], which are progressive neuropathies that get worse over time and can damage peripheral nerves and motor neurons, leading to weakness, numbness, and pain in the limbs.[1,2]

SORD Deficiency, is caused by mutations in the SORD gene leading to an inability to metabolize the sugar sorbitol. This results in the accumulation of high and toxic levels of sorbitol, causing significant disability, loss of sensory function and decreased mobility.[2,3]

Signs and Symptoms of SORD Deficiency

- Symptoms of SORD Deficiency typically occur between the ages of 9 and 25 but can start as early as age 2 or as late as age 40. Most people show symptoms around the age of 17.[2]
- When sorbitol builds up in blood and tissues it can cause tissue damage throughout the body.[2,3] Individuals with SORD Deficiency have approximately **100 times** the sorbitol concentration in their blood than unaffected individuals.[3]
- Excess toxic sorbitol can lead to various symptoms, which can worsen over time.[2]

MUSCLE WEAKNESS

At the time of diagnosis, the first symptom is ofter difficulty walking, which can range from mild (stumbling) to severe (progressing to needing a walker or wheelchair, and in some cases near paralysis).

98% will have weakness **IN THEIR LEGS**

59% will have weakness **IN THEIR ARMS**

SENSORY IMPAIRMENT

TWITCHING OR TREMOR

NEUROPATHIC PAIN

For more information about SORD Deficiency (CMT-SORD, SORD Neuropathy), please visit the Applied Therapeutics webpage here.

APPLIED THERAPEUTICS

REFERENCES

1. Applied Therapeutics. What is SORD Deficiency? Accessed March 2, 2022. https://www.appliedtherapeutics.com/patients-caregivers/sord-deficiency/
2. Cortese A, Zhu Y, Rebelo AP, et al. Biallelic mutations in SORD cause a common and potentially treatable hereditary neuropathy with implications for diabetes. Nat Genet 52(5):473-481. https://doi.org/10.1038/s41588-020-0615-4
3. Hereditary Neuropathy Foundation. SORD deficiency. Accessed March 2, 2022. https://www.hnf-cure.org/?s=SORD+deficiency&et_pb_searchform_submit=et_search_proccess&et_pb_include_posts=yes&et_pb_include_pages=yes
4. National Center for Biotechnology Information. PubChem compound summary for CID 5780, sorbitol. Accessed March 2, 2022. https://pubchem.ncbi.nlm.nih.gov/compound/Sorbito

How is SORD Deficiency Currently Managed?

- SORD Deficiency is primarily treated by neuromuscular specialists
- Traditional management focuses solely on monitoring and addressing symptoms, such as providing pain medicine, and using orthotics or surgery to address foot deformities
- Currently, there are no FDA-approved treatments for SORD Deficiency, but scientists are currently studying whether reducing levels of toxic sorbitol in the body could help treat SORD Deficiency

Why it is Important to Get Tested and Diagnosed

Genetic testing for SORD Deficiency is available through GeneDx, and found at the hyperlink here

- » Prior to 2020, people living with SORD Deficiency were diagnosed symptomatically as CMT2 or dHMN with an unknown genetic cause. However, with the recent discovery of the SORD gene, you can get genetically tested (or re-tested) to confirm if you have SORD Deficiency
- » Genetic testing should be performed on any patient, and any potentially affected family members, with CMT2 or dHMN of unknown genetic cause
- » If you have had genetic testing done in the past, it is recommended that you contact your healthcare provider and request a re-test that would include testing for the SORD gene

For Patients: Ask your doctor to order the SORD Deficiency genetic test through GeneDX. The genetic test can be run on a blood sample taken in the doctor's office, or via an at-home oral swab kit. It takes about 4-6 weeks to receive the test results.

For Healthcare Providers: GeneDx offers SORD Deficiency genetic testing. The single-gene test is offered through the GeneDx's provider portal. Simply scan the QR code above with your phone camera which will take you directly to the GeneDX portal or use the website address above to access the portal. Step-by-step directions are below:

1. Using the QR code or website link above, enter the GeneDx portal
2. Enter Test Code TG70 and the search result will open the Exome Slice Tool
3. Add "SORD" in the box for 'Enter Genes for Slice'
4. Click "Add these genes to your slice"
5. Click 'Order Slice for patient online via GeneDx'
6. It will then show you the SORD exome slice option - click 'Add to Cart'
7. HCP then enters patient information

For questions regarding SORD Deficiency genetic testing, please email SORD@AppliedTherapeutics.com

APPLIED THERAPEUTICS