AN INTRODUCTION TO SORD DEFICIENCY

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What is SORD Deficiency?

Sorbitol Dehydrogenase (SORD) Deficiency is a recently discovered rare, progressive genetic disease.[1]

People with SORD Deficiency are missing a key enzyme needed to process a substance called sorbitol.[2,3] Sorbitol is a sugar created in the body.[3,4] Without this necessary enzyme, sorbitol builds up and is toxic. This results in significant weakness and disability.[2,3]

- **Sorbitol** is a form of sugar found in many foods, drinks, and even certain medications.[4] In healthy individuals, the body converts sorbitol into fructose for energy.[3] Your body also makes sorbitol naturally on its own.[3,4]
- **SORD** is an enzyme that converts sorbitol into the sugar fructose within the body.[3] Sorbitol cannot be processed without this enzyme.[2,3]
- **When sorbitol is not able to be converted by the body,** it builds up and causes damage to cells and tissues throughout the body.[2,3]

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SORD Deficiency was discovered in 2020[2]

SORD Deficiency is a rare disease that affects approximately 1 in every 100,000 people. In the United States, it is estimated that there are 3,300 individuals living with the disease.[5]

Before the discovery of the SORD gene, people living with SORD Deficiency were diagnosed based on their symptoms as having Charcot-Marie-Tooth disease type 2 (CMT2) or distal hereditary motor neuropathy (dHMN).[2]

SORD Deficiency, CMT2, and dHMN are progressive neuropathies that get worse over time and can damage peripheral nerves and motor neurons, leading to weakness, numbness, or pain in the limbs.[1,2]

The recent discovery that disease symptoms in CMT2 and dHMN can be caused by deficiencies in the SORD enzyme now gives people living with SORD Deficiency and their physicians greater understanding of their specific disease.[2,3]

Neuropathy is damage or dysfunction of one or more nerves that typically results in numbness, tingling, muscle weakness, and pain in the affected area.[5] SORD Deficiency is the most frequent autosomal recessive form of hereditary neuropathy, which means that this disease is passed down from both parents' genes; however, not all people with SORD Deficiency have a family history of hereditary neuropathy.[2,3]

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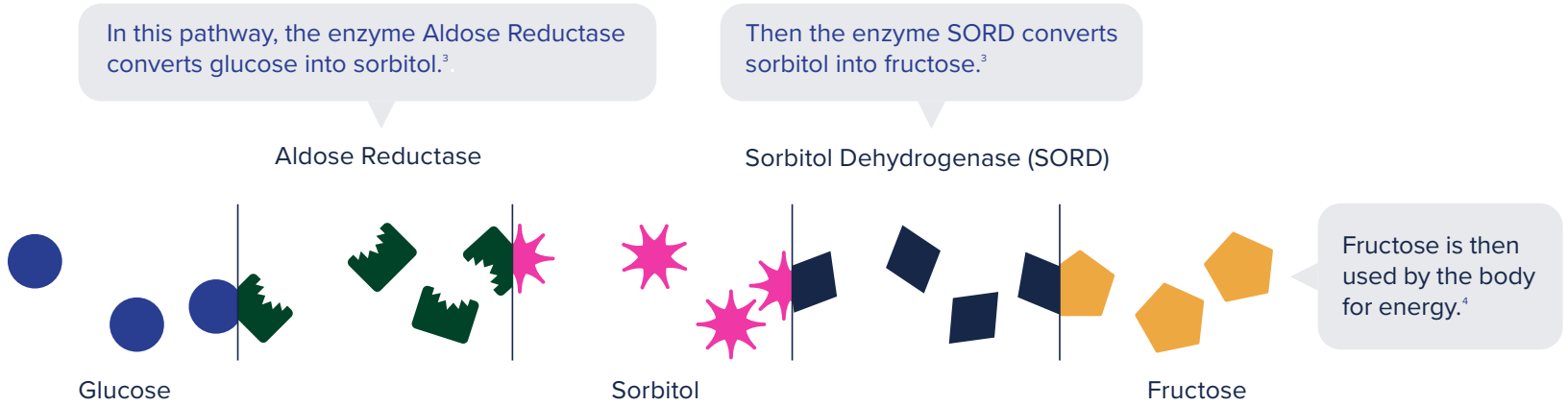
Sorbitol is converted by the body into fructose, which is used for energy[2.3]

Glucose is a form of sugar that the body converts into sorbitol, and then converts that sorbitol into fructose for energy.[3]

In healthy individuals

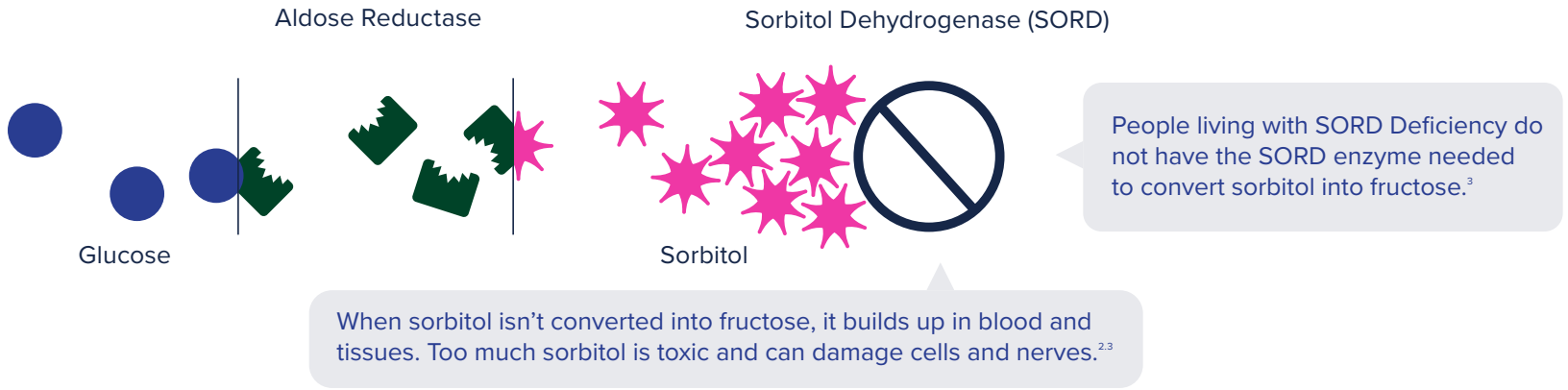
One of the ways the body breaks down glucose is through a 2-step process involving 2 enzymes[3]:

1. In the first step, the enzyme Aldose Reductase converts glucose into sorbitol
2. In the second step, the enzyme SORD converts sorbitol into fructose



People living with SORD Deficiency

1. Because the SORD enzyme is deficient, sorbitol builds up in the blood and tissues[2.3]
2. They **do not** produce the SORD needed to convert sorbitol into fructose[3]



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What happens when sorbitol builds up?

When sorbitol is not converted into fructose, it builds up in blood and tissues, causing damage throughout the body.[2,3] Individuals with SORD Deficiency have approximately **100 times** the sorbitol concentration in their blood than unaffected individuals.[3]

Neuromuscular symptoms in people living with SORD Deficiency are caused by toxic, high levels of sorbitol in the body.[2,3] 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]

Excess toxic sorbitol can lead to various symptoms, which can worsen over time.[2] Additional signs and symptoms of SORD Deficiency can include[2]:

MUSCLE WEAKNESS

98% will have weakness in their legs
59% will have weakness in their arms

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

TWITCHING/ TREMOR

SENSORY IMPAIRMENT

NEUROPATHIC PAIN

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How is SORD Deficiency currently managed?

Traditional management focuses solely on monitoring and addressing symptoms, such as providing pain medicine and using orthotics or surgery to address foot deformities.[2]

Right now, there are no FDA-approved treatments for SORD Deficiency.

Scientists are currently studying whether reducing levels of toxic sorbitol in the body could help to treat SORD Deficiency.

References:

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