A Guide To:

Succinic Semialdehyde Dehydrogenase Deficiency (SSADH)
Succinic semialdehyde dehydrogenase (SSADH) deficiency is an ultra-rare neurometabolic disorder characterized by the lack of one of two enzymes involved in the breakdown of GABA, the major inhibitory neurotransmitter in the brain. GABA controls the movements of humans, and when it is imbalanced, major neurological abnormalities occur. With SSADH, neurotransmitters in neurons are blocked from signaling one another correctly.

Due to the enzyme deficiency in SSADH patients, an unusual compound accumulates in the body, namely 4-hydroxybutyric acid or gamma-hydroxybutyric acid (GHB). The GHB accumulation may interfere with the patient’s ability to walk, speak, concentrate and process information.

Since the disorder was originally described in 1981 by Cornelis Jakobs, PhD. over 200 cases of SSADH have been identified. SSADH appears to affect males and females equally.

However, due to the variability and nonspecific nature of associated symptoms, experts suggest that this disorder may be significantly underdiagnosed and/or misdiagnosed. As a result, it is difficult to determine the true frequency of SSADH in the general population.

A good reference to find additional information about SSADH is on the National Institutes of Health web site at the address below, searching on succinic semialdehyde dehydrogenase deficiency or SSADH Deficiency.

www.nih.gov


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According to reports in the medical literature, initial or “presenting” symptoms vary from case to case. However, initial symptoms often include delays in achieving certain motor milestones (e.g., crawling, sitting unaided, walking without assistance); reduced muscle tone (hypotonia); and/or intellectual or language delays.

In some cases, additional presenting symptoms may be present, such as ataxia causing an impaired ability to coordinate voluntary movements; episodes of uncontrolled electrical activity in the brain or seizures; and/or certain abnormalities during early infancy, including failure to cry or respond to certain visual stimuli. Although symptom onset is usually detected during infancy or childhood, the disorder sometimes does not get diagnosed until later in life, and infrequently not until adulthood.

Symptoms associated with SSADH may be mild, moderate or severe and often vary greatly from case to case even within the same family. The symptoms of SSADH are caused by the accumulation of GABA and GHB in the brain and include the following manifestations:

(Defined as: common, > 70% of patients; frequent 30-70% of patients; unusual, < 30% of patients)

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SSADH is inherited as an autosomal recessive trait. In recessive trait disorders, the condition does not occur unless an individual inherits one copy of the same defective gene for the same trait for SSADH from each parent. With each pregnancy the couple has a 25% chance of this occurring.

Likewise, the couple has a 25% percent chance of their children receiving both normal genes for the same trait from each parent and would have no symptoms and will not pass the disorder on to their children.

Additionally, the couple has a 50 percent chance of their children being a carrier of the disorder, but will have no SSADH symptoms that we are aware of.
The diagnosis of SSADH is usually made after birth (postnatally) during infancy or childhood (or, in some cases, later in life), based upon a thorough clinical evaluation, identification of characteristic physical findings, and a variety of specialized tests.

Due to the nonspecific nature and variability of associated symptoms, experts suggest that SSADH should be considered in any individuals with two or more features of intellectual, language, and motor delay and abnormally diminished muscle tone (hypotonia) of unknown cause (idiopathic).

Specialized testing to confirm a diagnosis of SSADH typically includes studies (i.e., quantitative organic acid analysis in an appropriate specialist laboratory) that may detect increased concentrations of 4-hydroxybutyric acid (4-HBA) in urine (i.e., 4-hydroxybutyric aciduria) and molecular genetic testing to confirm the abnormal gene from each parent in the patient. (Note: As mentioned above, increased concentrations of 4-HBA may also be detected in plasma and cerebrospinal fluid. In addition, deficient SSADH activity has also been demonstrated in certain cells other than eukocytes.)

ALDH5A1 is the gene that codes for SSADH. Molecular genetic testing to identify bi-allelic mutations (abnormal changes found on both copies of a gene) or deletions in ALDH5A1 is used to make or confirm a diagnosis of SSADH. This testing is usually ordered by the patient’s pediatrician, primary care physician, neurologist or a genetic counselor and can be completed at a number of facilities around the world. However, it is imperative that the testing facility specifically test for ALDH5A1. Fortunately, diagnostic capabilities to identify SSADH via gene sequencing have been enhanced because a number of companies assess the sequence of this gene on panels of genes for idiopathic developmental delay, epilepsy, and other clinical features.
The treatment of SSADH is directed toward the specific symptoms that are apparent in each individual. Such treatment may require the coordinated efforts of a team of medical professionals, such as a pediatrician or a primary care physician, pediatric neurologist or adult neurologist who specialize in the diagnosis and treatment of neurological disorders and/or other health care professionals. Additionally, genetic counseling will be of benefit for affected individuals and their families.

In some affected individuals, treatment may include the use of certain medications to help prevent, reduce, or control seizures (anticonvulsants, e.g., carbamazepine, levetiracetam, etc.) or to alleviate other behavioral symptoms potentially associated with the disorder.

Early intervention is important in ensuring that patients with SSADH reach their potential. Special services that may be beneficial include physical therapy, speech therapy, occupational therapy, special remedial education, and other medical, social, and/or vocational services. There are a number of other therapies available depending on where you live and the needs of your patient. Some examples are hippo therapy (horseback riding), music therapy, sensory integration therapy, animal-assisted therapy, etc.
Patients and families interested in obtaining information about the latest therapeutic and/or research information on SSADH may wish to contact:

**SSADH Association**  
**Carolyn Hoffman**  
P.O. Box 180622  
Delafield, WI 53018 USA  
Phone: (262) 646-5133  
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Physicians interested in obtaining clinical and/or therapeutic and research information on SSADH may wish to contact:

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PhD’s interested in obtaining research information on SSADH may wish to contact:

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<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Institution</th>
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<tbody>
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SSADH Community

The SSADH community is an amazing group of patients, families, scientists and doctors. Though we are few in number and spread out around the world we share a common challenge and work towards making a better life for this very special patient population.

The SSADH Association continues to work diligently to move research forward and has been doing so since 1998. Gratefully, we are supported by a team of research scientists and medical professionals who have devoted the majority of their careers to finding a therapeutic solution to this disorder. Their unwavering support, guidance and determination have given endless hope to all the SSADH families. It is because of their extraordinary efforts that they have been awarded grants from the National Institutes of Health and private charitable funds enabling their continued research. Many of these grants are unheard of for an ultra-rare disorder like SSADH.

SSADH Chip for Charity

Since 1998, the Chip for Charity Golf Outing is held in Richfield, Wisconsin in order to raise money for SSADH research. Each year friends and family members take time out from their busy schedules to participate in this event. The day includes golf, hole contests, lunch, raffle prizes, happy hour, dinner and a silent auction.

The Chip for Charity involves hundreds of golfers, countless donations and many generous sponsorships, as well as a team of dedicated volunteers to make the day a success.

This event held each September is the primary funding source of the SSADH Association. However, we need all families to continue to spread the word and round up donations. The more we are able to raise awareness the more likely we are to find more patients and a therapeutic solution for this disorder!

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