UNDERSTANDING AADC DEFICIENCY

When your child's low muscle tone (hypotonia) goes unexplained, a rare genetic disorder may be the cause.

Learn more about Aromatic L-amino Acid Decarboxylase (AADC) deficiency, which can cause hypotonia and other symptoms in children.

Intended for general disease awareness information.
Please refer to your child's doctor for further information.

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WHAT IS AADC DEFICIENCY?

Aromatic L-amino Acid Decarboxylase (AADC) deficiency is a rare genetic disorder that affects the brain, causes weak muscle tone, and affects how a child develops.

Genetic disorders are caused by an alteration (mutation) in genes.

Genes are found within cells and are made up of DNA. They carry information that determines the traits and characteristics passed down to individuals from their parents. These genes influence how a person looks, including skin, hair, and eye color.

Genes also provide instructions to make building blocks called proteins, such as enzymes. These proteins help to support important functions in the body like digestion, communication between different parts of the body, energy production, and growth.

Sometimes there can be an alteration within a gene, called a genetic mutation. This change can be harmful and lead to genetic health problems or disorders, like AADC deficiency.

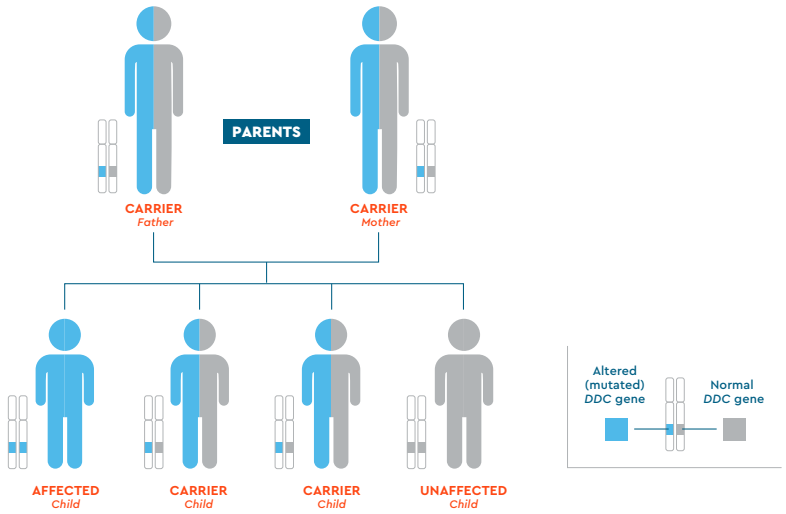
HOW IS AADC DEFICIENCY PASSED DOWN?

Our genes come from our parents. Each person gets 2 copies of every gene, 1 from each parent. Copies of genes can be working copies, or altered copies that do not work as they are supposed to (mutated copies).

AADC deficiency is inherited, or passed down, from a person's parents. In order for a person to have AADC deficiency, both mother and father carry an altered (mutated) copy of the dopa decarboxylase (*DDC*) gene. Each parent then has to pass down 1 altered copy of the *DDC* gene to the child, so the child has 2 altered copies.

This is known as an autosomal recessive disorder, or a disorder that occurs when a person inherits 2 altered copies of a gene, 1 from the mother and 1 from the father.

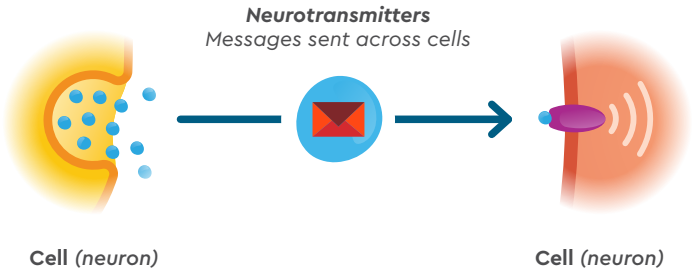
How AADC deficiency is inherited



WHAT CAUSES AADC DEFICIENCY?

AADC deficiency is caused by an alteration in a gene called the *DDC* gene.

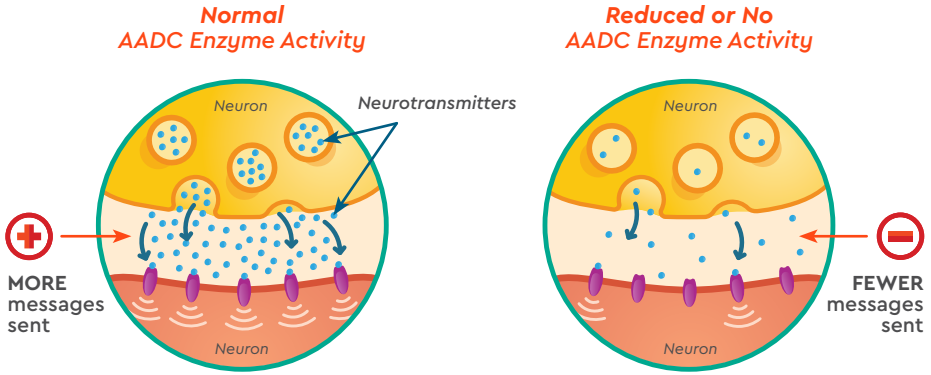
There is a gene in the body called the *DDC* gene that is needed to make an enzyme called AADC. The AADC enzyme helps to make natural chemicals called neurotransmitters.



Neurotransmitters are the messages sent between the cells in the nervous system called neurons. Neurons send and receive messages that are important for controlling different functions in the body, including the senses and motor function. These messages are important because they help to control many of the body's functions.

WHAT HAPPENS IN AADC DEFICIENCY?

AADC deficiency is a disorder that interferes with the way the cells in the nervous system talk to each other.



- In AADC deficiency, an alteration (mutation) within the *DDC* gene leads to a **decrease or no activity of the AADC enzyme**
- This results in a **lower level of or no neurotransmitters**
  - In AADC deficiency, the neurotransmitters called dopamine and serotonin are most affected
- Without enough neurotransmitters (messages), **neurons can't communicate with each other**
- This means that the **body can't perform important functions** and can result in the symptoms of AADC deficiency that limit daily life

SIGNS AND SYMPTOMS OF AADC DEFICIENCY

The decrease in neurotransmitters (natural chemicals that send messages in the nervous system) that is caused by AADC deficiency may result in a range and severity of symptoms.

The most common symptoms include:

- Low muscle tone, sometimes called hypotonia or "floppy baby" *(Figures A, B)*
- Delays in development, such as the ability to:
  - Lift and control their head
  - Crawl, sit, or stand without support
  - Babble or say words
  - Walk
- Increased tightness of muscle tone and reduced ability of the muscle to stretch
- Movement problems, including:
  - Involuntary muscle contractions, sometimes called dystonia *(Figure C)*
  - Involuntary eye movements called oculogyric crises *(Figures D, E)*
    - Involuntary movements may accompany an episode, including contracting muscles and/or twisting

People with AADC deficiency may also show signs of:

- Other involuntary movements, such as sudden jerking, flailing, or twisting
- Excessive sweating (sometimes called diaphoresis)
- Drooling
- Drooping eyelids
- Stuffy or runny nose

These symptoms may also be present:

- Seizures (a sudden rush of electrical activity to the brain)
- Sleeping problems
- Irritability
- Excessive crying
- Problems with digestion
  - Diarrhea
  - Constipation
  - Reflux
- Problems with feeding

Each individual is different, so not every person will have every symptom and the severity of symptoms will vary from person to person.

THE CHALLENGE OF A CORRECT DIAGNOSIS

Although symptoms are often seen when the person is still an infant, an accurate diagnosis may take a long time. AADC deficiency is rare and many of its symptoms are similar to other disorders, so it is often misdiagnosed or not diagnosed.

AADC deficiency may be misdiagnosed as these conditions because they have similar symptoms:

- Epilepsy
- Neuromuscular disorders
- Cerebral palsy
- Juvenile parkinsonism
- Mitochondrial disease
- Behavioral disorders/autism

When AADC deficiency is misdiagnosed at first or is never correctly diagnosed, treatment and proper management of this condition is delayed.

TELLING AADC DEFICIENCY APART FROM OTHER CONDITIONS

These are signs and symptoms that may set AADC deficiency apart from other conditions:

Involuntary eye movements called oculogyric crises
Episodes when a child's eyes suddenly roll upward, without control, that can last anywhere from a few seconds to hours, and can happen several times a day or several times a week

Normal brain scans

Multiple symptoms associated with bodily functions such as excessive sweating, droopy eyelids, and a stuffy or runny nose

Symptoms may become worse or more noticeable later in the day and improve with sleep

If your child is showing 1 or a combination of these signs and symptoms, you may want to talk to your child's doctor about screening for AADC deficiency.

GETTING YOUR CHILD TESTED FOR AADC DEFICIENCY

To get an accurate diagnosis, your child's doctor may perform multiple tests that are not specific for AADC deficiency, but can help identify problems in the brain, such as:

- **MRI:** a test that uses a magnetic field and radio waves to create detailed images of the body's organs and structures
- **CT:** a scan that uses a series of X-ray images taken from different angles around the body and uses computer processing to create images of organs, bones, and other tissues, allowing a doctor to see inside the body
- **EEG:** a test that looks at abnormalities in the brain's activity by attaching small metal sensors to the scalp in order to detect tiny electrical activity from the brain

Doctors may perform additional tests if some of these test results do not give clear answers.

Core tests to diagnose AADC deficiency include:

- **Blood test for 3-OMD**: This simple screening test measures a compound called 3-OMD that can be useful if your child's doctor suspects AADC deficiency. The following tests can be performed to confirm a diagnosis

A positive result from 2 or more of the following tests confirm a diagnosis of AADC deficiency.

- **Genetic testing:** Your child's doctor may recommend genetic testing to look more closely at the *DDC* gene
- **Blood test for AADC enzyme activity:** This test measures the activity of the AADC enzyme, which is reduced in patients with AADC deficiency
- **CSF neurotransmitter metabolite panel:** Neurotransmitters allow the cells in the nervous system to talk to each other. This test measures the levels of different compounds (metabolites) involved in the making of neurotransmitters

Your child's doctor will work with you to explain what kind of sample is needed for each individual test.

CT scan=computed tomography scan; EEG=electroencephalogram; MRI=magnetic resonance imaging; 3-OMD=3-O-methyldopa; CSF=cerebrospinal fluid; DDC=dopa decarboxylase.

ASK YOUR CHILD'S DOCTOR IF YOU SUSPECT YOUR CHILD MAY HAVE AADC DEFICIENCY

Aromatic L-amino Acid Decarboxylase (AADC) deficiency is a rare genetic disorder that affects the brain, causes weak muscle tone, and affects how a child develops.

- AADC deficiency is inherited, or passed down, from a person's parents
- The most common symptoms of AADC deficiency include low muscle tone, delays in development, and movement disorders, especially oculogyric crises
- Oculogyric crises, normal brain scans, multiple symptoms associated with bodily functions, and symptoms that worsen or become more noticeable at night can help to differentiate AADC deficiency from other disorders
- Your child's doctor may recommend various tests, including genetic testing, to confirm or rule out AADC deficiency

Ask your child's doctor for more information about this disorder and testing if you suspect your child has AADC deficiency.

This disease awareness leaflet has been funded and developed by PTC Therapeutics.

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