ADNP-related syndrome
- or -
Helsmoortel-Van der Aa syndrome
This guide is not meant to take the place of medical advice.

Please consult with your doctor about your genetic results and health care choices. The information in this guide was up to date at the time it was written in 2019. But new information may come to light with new research. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has ADNP-related syndrome.
What is ADNP-related syndrome?

ADNP-related syndrome happens when there are changes to the ADNP gene. These changes can keep the gene from working as it should. The syndrome is also known as Helsmoortel-Van der Aa syndrome.

Key role
The ADNP gene plays a key role in the brain and body, including the heart and intestines.

Symptoms
Because the ADNP gene is important in the development and function of brain cells, many people who have ADNP-related syndrome have:

- Developmental delay, or intellectual disability, or both
- Speech and language delay
- Autism or symptoms of autism
- Other behavior issues
- Distinctive facial features
- Intestinal problems or difficulty eating
- Heart problems
- Vision problems
- Sleep difficulties
- Seizures
What causes ADNP-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the ADNP gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. In most cases, parents pass on exact copies of the gene to their child. But the process of copying genes is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

Sometimes a random change happens in the sperm or egg. This change to the genetic code is called a ‘de novo’, or new, change. The child can be the first in the family to have the gene change.
De novo changes can take place in any gene. We all have some de novo changes, most of which don’t affect our health. But because ADNP plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that ADNP-related syndrome is often the result of a de novo change in ADNP. Many parents who have had their genes tested do not have the ADNP gene change found in their child who has the syndrome. In some cases, ADNP-related syndrome happens because the gene change was passed down from a parent.
Why does my child have a change in the ADNP gene?

No parent causes their child's ADNP-related syndrome. We know this because no parent has any control over the gene changes that they do or do not pass on to their children. Please keep in mind that nothing a parent does before or during the pregnancy causes this to happen. The gene change takes place on its own and cannot be predicted or stopped.

What are the chances that other family members of future children will have ADNP-related syndrome?

Each family is different. A geneticist or genetic counselor can give you advice on the chance that this will happen again in your family.

The risk of having another child who has ADNP-related syndrome depends on the genes of both birth parents.

- If neither birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is on average 1 percent. This 1 percent chance is higher than the chance of the general population. The increase in risk is due to the very unlikely chance that more of the mother’s egg cells or the father’s sperm cells carry the same change in the gene.
- If one birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has ADNP-related syndrome, the risk of having a child who has the syndrome depends on the symptom-free sibling’s genes and their parents’ genes.

- If neither parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child who has ADNP-related syndrome.
- If one birth parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a small chance of also having the same gene change. If the symptom-free sibling has the same gene change as their sibling who has the syndrome, the symptom-free sibling’s chance of having a child who has ADNP-related syndrome is 50 percent.

For a person who has ADNP-related syndrome, the risk of having a child who has the syndrome is about 50 percent.
How many people have ADNP-related syndrome?

As of 2019, about 80 people in the world with changes in the ADNP gene have been described in medical research. The first case was described in 2014. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have ADNP-related syndrome look different?

People who have ADNP-related syndrome may look different. Appearance can vary and can include some but not all of these features:

- Enlarged forehead and high hairline
- Wide bridge of nose
- Cup-shaped ears that stick out
- Differences in the appearance of hands, including extra fingers, also called polydactyly
How is ADNP-related syndrome treated?

Scientists and doctors have only just begun to study ADNP-related syndrome. At this point, there are no medicines designed to treat the syndrome. A genetic diagnosis can help people decide on the best way to track the condition and manage therapies. Doctors can refer people to specialists for:

- Physical exams and brain studies
- Genetics consults
- Development and behavior studies
- Other issues, as needed

A developmental pediatrician, neurologist, or psychologist can follow progress over time and can help:

- Suggest the right therapies. This can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for ADNP-related syndrome should begin as early as possible, ideally before a child begins school.

If seizures happen, consult a neurologist. There are many types of seizures, and not all types are easy to spot. To learn more, you can refer to resources such as the Epilepsy Foundation's website: epilepsy.com/learn/types-seizures.
ADNP-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies found around 80 people who have ADNP-related syndrome.

This section includes a summary of information from major published articles. It highlights how many people have different symptoms. To learn more about the articles, see the Sources and references section of this guide.

Behavior and development concerns linked to ADNP-related syndrome

Behavior

Almost everyone who has the syndrome has autism or symptoms of autism. Some people who have the syndrome also have anxiety, obsessive compulsive disorder, aggressive behavior, temper tantrums, attention deficit hyperactivity disorder, also called ADHD, and sleep problems.

Speech

Almost everyone who has the syndrome has speech delay. Children are often late to start talking and may have a limited vocabulary.

Learning

Most people have some level of intellectual disability, ranging from mild to severe, and will need special educational support.
Muscle tone

Three-quarters of people have low muscle tone, also called hypotonia. This can lead to delays in sitting and walking.

Sitting and walking

Children often sit and walk late. According to one study of 11 children, children first sat without help between 7.5 months and 12 months of age and started walking between 19 months and 4.5 years of age.

Feeding and digestion issues

Eating difficulties are common. People may also have vomiting, constipation, and heartburn or reflux.

8 out of 12 people have difficulty eating

Immune system

Almost two-thirds have repeated infections, including colds and urinary tract infections.

7 out of 11 people have repeated infections
Medical and physical concerns linked to ADNP-related syndrome

Growth
Some children have growth delay and may be shorter than their peers. About one-half (4/7) have increased weight around the midsection.

Birth defects
One-quarter of people are born with heart defects, including a hole in the heart, also called atrial septal defect, and leakage of blood between two heart chambers, also called mitral valve prolapse.

Eyes and eyesight
More than one-half of those who have ADNP-related syndrome have vision problems, typically farsightedness or crossed eyes.

Brain
Some have differences in the structure of the brain, as shown by an MRI scan, which generates a picture of the brain. Scientists don’t yet know how these differences affect people. A small number of people (2/12) have seizures.

3 out of 12 people have heart defects
Simons Searchlight is another research program sponsored and run by the Simons Foundation Autism Research Initiative, also known as SFARI. As part of the next step in your research journey, Simons Searchlight offers you the opportunity to partner with scientists and other families who have the same gene change. Simons Searchlight is a registry for more than 150 genetic changes that are associated with neurodevelopmental conditions, including autism spectrum disorder. Simons Searchlight makes it easier for researchers to access the information they need to advance research on a condition.

To register for Simons Searchlight, go to the Simons Searchlight website at www.simonssearchlight.org and click “Join Us Today”.

- Learn more about Simons Searchlight
  www.simonssearchlight.org/frequently-asked-questions

- Simons Searchlight webpage with more information on ADNP
  www.simonssearchlight.org/research/what-we-study/adnp

- Simons Searchlight Facebook group
  www.facebook.com/groups/searchlight.ADNP
Sources and References

The content in this guide comes from published studies about ADNP-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.
