MBD5-associated neurodevelopmental disorder or MAND
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 MBD5-associated neurodevelopmental disorder.
What is MBD5-associated neurodevelopmental disorder?

MBD5-associated neurodevelopmental disorder is a group of conditions that happen when there are changes to the MBD5 gene. These changes can keep the gene from working as it should. The disorder is also known as MAND.

MAND can happen when there are changes to the MBD5 gene. The disorder can also happen when larger segment of DNA are deleted or duplicated. Then it is known as 2q23.1 deletion syndrome or 2q23.1 duplication syndrome.

Key role
The MBD5 gene plays a key role in the development and function of the brain. It is also important for other organs, including the heart and intestines.

Symptoms
Because the MBD5 gene is important in the brain, many people who have MAND have:

- Intellectual disability
- Motor delay
- Speech impairments
- Seizures
- Autism spectrum disorder
- Behavior issues, including sleep issues, repetitive behaviors, and short attention span
Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the MBD5 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 MBD5 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that MAND is often the result of a de novo change in MBD5. Many parents who have had their genes tested do not have the MBD5 gene change found in their child who has the disorder. In some cases, MAND happens because the gene change was passed down from a parent. This is called dominant inheritance.
Why does my child have a change in the MBD5 gene?

No parent causes their child's MAND. 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 or future children will have MAND?

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 MAND 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 disorder 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 disorder is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has MAND, the risk of having a child who has the disorder 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 disorder, the symptom-free sibling has a nearly 0 percent chance of having a child who has MAND.

- If one birth parent has the same gene change found in their child who has the disorder, 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 disorder, the symptom-free sibling’s chance of having a child who has MAND is 50 percent.

For a person who has MAND, the risk of having a child who has the disorder is about 50 percent.
How many people have MAND?

As of 2019, about 100 people in the world with changes in the MBD5 gene had been described in the medical literature. The gene was linked to autism in 2011. Scientists expect to find more people who have the disorder as access to genetic testing improves.

Do people who have MAND look different?

Most people who have MAND don't look very different. Appearance can vary and can include some but not all of these features:

- Broad forehead
- Thick or highly arched eyebrows
- Changes to the outer ear, such as a forward-facing structure
- Large earlobes, ears that stick out, or ears that are cupped
- Short nose, depressed or wide nasal bridge
- Downturned corners of the mouth and thin upper lip
How is MAND treated?

Scientists and doctors have only just begun to study MAND. At this point, there are no medicines designed to treat the disorder. 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. These can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for MAND 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: [www.epilepsy.com/learn/types-seizures](http://www.epilepsy.com/learn/types-seizures).
MAND is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies described around 100 people who have MAND.

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 MAND

Speech

Almost all children who have MAND have speech impairments. Most children lack speech entirely or have single words or short sentences.

Learning

Most children who have MAND have some intellectual disability, ranging from mild to severe. Many need special educational support.

Behavior

Many people who have MAND have autism or features of autism.

About 80 percent of people have short attention span and repetitive behaviors.

About 80 percent of people have sleep problems. This can include nighttime waking, night terrors, and waking in the early hours of the morning. Many have excessive daytime sleepiness.

About 60 percent are aggressive and may harm themselves.

Less than 10 percent have anxiety, hyperactivity, inappropriate happy demeanor and social withdrawal.
Medical and physical concerns linked to MAND

Feeding and digestion issues
Problems with feeding and constipation are common. This is likely linked to low muscle tone.

Brain
Many people who have MAND have seizures. The type of seizures can include:

- Absence spells
- Generalized tonic-clonic, which are seizures that involve the entire body
- Atonic, also called a drop seizure, a type of seizure accompanied by a sudden loss of muscle tone
- Sleep related seizures
- Startle-induced atonic seizures

About 80% of children who have MAND have seizures.

Sitting and walking
Children who have MAND often have delays in development of large motor skills and fine motor skills. The average age of walking is 2 years to 3 years.

About 70% of people have poor coordination and broad-based or uncoordinated walking.
Medical and physical concerns linked to MAND

Muscle tone
Many people who have MAND have low muscle tone.

Joints and spine
People who have MAND often have skeletal issues.

One study of 65 people found that 75 percent had small hands and feet. About 40 percent had a curved fifth finger or short fifth digit on the hands and feet. 33 percent of people had a wide space between their first and second toes.

Heart
Heart problems were seen in 10 percent of people. These problems include openings in the upper chambers of the heart, also called atrial septal defect, or the lower chambers of the heart, also called ventricular septal defect. People also had issues with a specific heart valve, the pulmonary valve, also called pulmonary valve stenosis.
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 200 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 MBD5  
  www.simonssearchlight.org/research/what-we-study/MBD5

- Simons Searchlight MBD5 Facebook community  
  www.facebook.com/groups/searchlight.MBD5
Sources and References

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

  www.ncbi.nlm.nih.gov/pubmed/23422940

- Hodge JC. et al. Molecular Psychiatry, 19, 368-379, (2014). Disruption of MBD5 contributes to a spectrum of psychopathology and neurodevelopmental abnormalities
  www.ncbi.nlm.nih.gov/pubmed/23587880

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