Neurofibromatosis type 2
Also called: NF-2, NF2, bilateral acoustic neurofibromatosis, central neurofibromatosis, familial acoustic neuromas

What is neurofibromatosis type 2?
Neurofibromatosis type 2 is a genetic condition that mainly affects the nervous system. People with neurofibromatosis type 2 are at increased risk to develop tumors within their nerves. The most common type of tumor in people with neurofibromatosis type 2 is vestibular schwannoma (also known as acoustic neuroma). Vestibular schwannomas develop along the nerve that carries information from the inner ear to the brain (the auditory nerve). In patients with neurofibromatosis type 2, vestibular schwannomas usually develop on both auditory nerves at an average age of 18 to 24 years. Almost all patients with neurofibromatosis type 2 will develop bilateral (both-sided) vestibular schwannomas by 30 years of age.

Tumors in other parts of the nervous system can also develop. These include the following:

- Meningiomas—tumors on the membranes surrounding the brain and spinal cord
- Ependymomas—tumors that form in fluid-producing cells of the brain or spinal cord
- Astrocytomas—tumors that form in supportive tissue in the brain or spinal cord
- Retinal hamartomas—tumors that form in the back of the eye

Cataracts and other eye problems are also common in people with neurofibromatosis type 2.

Neurofibromatosis type 2 is hereditary, which means it can be passed from parents to their children. How severe the signs and symptoms of this condition are may vary between families. However, people with neurofibromatosis type 2 who are in the same family often have a disease course that is similar.

How is neurofibromatosis type 2 diagnosed?
A diagnosis of neurofibromatosis type 2 can be made with or without genetic testing. Genetic testing can be offered to people who have features that suggest neurofibromatosis type 2 to confirm the diagnosis.

For a person without a known family history of neurofibromatosis type 2, any one of the following confirms a clinical diagnosis of the condition:

- Bilateral (both-sided) vestibular schwannoma tumors
- Unilateral (one-sided) vestibular schwannoma tumor, plus any two of the following:
  - Meningioma
  - Schwannoma
Glioma
- Neurofibroma
- Cataract

- Multiple meningiomas, plus one of the following:
  - Unilateral vestibular schwannoma
  - Any two of these: schwannoma, glioma, neurofibroma or cataract

For a person with a known family history of neurofibromatosis type 2, any one of the following confirms a clinical diagnosis of the condition:

- Vestibular schwannoma (unilateral or bilateral)
- Any two of these: meningioma, schwannoma, glioma, neurofibroma or cataract

**What is the tumor risk for people with neurofibromatosis type 2?**

Nearly all people with neurofibromatosis type 2 develop some type of tumor within the nervous system. The tumors usually develop along nerves in the brain and spinal cord, and sometimes in other parts of the body. The tumors are almost always noncancerous, but often they must be removed because they can cause problems.

<table>
<thead>
<tr>
<th>Type of Tumor</th>
<th>Lifetime Chance of Developing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular schwannoma (unilateral or bilateral)</td>
<td>95%</td>
</tr>
<tr>
<td>Meningioma</td>
<td>80%</td>
</tr>
<tr>
<td>Spinal tumors (schwannomas, astrocytomas and ependymomas)</td>
<td>66%</td>
</tr>
<tr>
<td>Retinal hamartoma</td>
<td>33%</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>rare</td>
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</tbody>
</table>

In some cases, the tumors may change and behave like cancers, but the risk of this is low. Doctors do not know what the exact risk of the tumors becoming cancerous is because it happens only very rarely.

**What are other features seen in people with neurofibromatosis type 2?**

Neurofibromatosis type 2 can affect many areas of the body. People with this condition may have some or all of the following features. Many of these are caused by the growth of tumors and irritation or damage to the nerves that are involved:

- Hearing loss
- Tinnitus (ringing in the ears)
- Feeling dizzy
- Headache
- Seizures
• Trouble with balance
• Poor vision or blindness
• Squinting of one or both eyes
• Trouble controlling the muscles of the face
• Problems lifting the hands or feet
• Weakness in the limbs

What causes neurofibromatosis type 2?
Neurofibromatosis type 2 is caused by changes in a gene known as \textit{NF2}. Genes carry information telling cells within the body how to function. The \textit{NF2} gene helps to control how and when cells grow, divide and die.

People without neurofibromatosis type 2 carry two working copies of the \textit{NF2} gene in their cells. One copy of \textit{NF2} is inherited from the mother and one from the father. Cells from people with neurofibromatosis type 2 carry one working copy of \textit{NF2} and one copy that is changed. This change causes the gene to not work properly. It is called an \textit{NF2} mutation.

About half of children with neurofibromatosis type 2 inherit the \textit{NF2} gene mutation from a parent who also has the syndrome. The other half of children with neurofibromatosis type 2 have a new \textit{NF2} mutation that did not come from a parent. These children have no history of the syndrome in their family. In these cases, the change either happened in an egg or sperm cell when the child was formed or in one of the child’s cells during pregnancy. These children are the first in their families to have neurofibromatosis type 2. No matter how they acquired the \textit{NF2} mutation, people with neurofibromatosis type 2 have a 50% or 1 in 2 chance of passing it on to their children.

As people with neurofibromatosis type 2 get older, the remaining working copy of \textit{NF2} often becomes changed within some of their cells. When both copies of the gene are changed, tumors can develop. Researcher believe this is why people with neurofibromatosis type 2 have a higher risk of developing tumors than people who do not have this condition.

Mosaic Neurofibromatosis 2
About 25 to 30 percent of people with no family history of neurofibromatosis type 2 have mosaic type neurofibromatosis 2 (sometimes called segmental neurofibromatosis 2). This means that the person has two different sets of cells that make up the body. One set contains two working copies of the \textit{NF2} gene. These cells are normal. The other set of cells contains one working and one non-working \textit{NF2} gene. These cells are abnormal.

During pregnancy, a person with mosaic neurofibromatosis type 2 inherits two normal copies of the \textit{NF2} gene, one from the mother and one from the father. However, early in development, one of the copies of the \textit{NF2} gene becomes mutated (changed) within one cell of the developing baby. That cell will continue to grow and divide, making many more cells in the baby’s body. All of the cells that grow from that early cell will also have the mutated
copy of the *NF2* gene. Other cells that did not grow from the one mutated cell will have two normal copies of the *NF2* gene. That is why it is called mosaic neurofibromatosis 2, because the person’s body is a mixture of normal cells and mutated cells.

With mosaic neurofibromatosis type 2 it is hard to know which cells have the *NF2* mutation, so it is not possible to predict the exact risk of passing the *NF2* mutation on to future children. The risk is up to 50% or a 1 in 2 chance of passing the *NF2* mutation onto each child.

People with mosaic neurofibromatosis type 2 generally only have features of the condition in the areas of the body that contain the *NF2* mutation.

**How are people with neurofibromatosis type 2 screened for tumors?**

People with neurofibromatosis type 2 should be managed by a doctor knows this condition well. Although most of the tumors related neurofibromatosis type 2 are not cancerous, people with the condition should be monitored for tumors. Some non-cancerous tumors can cause problems, such as loss of hearing or nerve damage. It is also important for doctors to carefully monitor tumors for signs that might mean they have become cancerous. The goal of screening is to find and treat tumors early to allow the best outcome for patients.

**Recommended screenings for children with neurofibromatosis type 2:**

- **Yearly physical exams** by a doctor who knows the condition well
- **Annual MRI scans of the brain** starting at 10 years of age and continuing until at least 40 years of age
- **MRI scan of the spine** starting at diagnosis and repeated if symptoms of a spinal tumor develop
- **Annual vision screening** by an ophthalmologist (eye specialist) starting at the time of diagnosis
- **Annual hearing evaluation** by an audiologist starting at the time of diagnosis

It is possible that recommended screenings may change over time as doctors learn more about neurofibromatosis type 2. Parents should discuss all screening options for their child with a doctor who knows this condition well. Because neurofibromatosis type 2 is a complex condition, it is very important that parents seek out an experienced doctor for their child.

**How is genetic testing for neurofibromatosis type 2 done?**

The doctor may suspect Neurofibromatosis type 2 after looking at a person’s medical or family history. In most cases, a doctor or genetic counselor will ask questions about a person’s health and the health of other family members.
The genetic counselor or doctor will record which family members have developed tumors, what types of tumors and at what ages tumors occurred. From this information they will create a family tree. Doctors and genetic counselors will look at the family tree to find out:

- If the types of tumors match up with what might be seen in those with neurofibromatosis type 2, and
- If there are family members who have clinical signs of neurofibromatosis type 2.

If neurofibromatosis type 2 is suspected in a child or other family members, the doctor or genetic counselor will likely recommend genetic testing of the \( NF2 \) gene.

**Diagnostic genetic testing**

If the doctor or genetic counselor suspects that a person has neurofibromatosis type 2, diagnostic testing may take place as follows:

- A blood sample is collected.
- DNA is isolated from the cells in the sample. A person’s genes are made of DNA.
- Both copies of the person’s \( NF2 \) gene are checked for possible changes. A genetic specialist compares the two copies of the patient’s gene to a normal \( NF2 \) gene. If there are differences, the specialist decides if these changes might cause neurofibromatosis type 2.
- If an \( NF2 \) mutation is found, the genetic counselor will work with the family in the following ways:
  - To help the family understand the cancer risks of neurofibromatosis type 2
  - To find out if other family members should consider testing for the mutation
  - To help with decisions about prenatal genetic testing

It is important to remember that genetic testing only finds a mutation in the \( NF2 \) gene for about 90 to 95 percent of people with neurofibromatosis type 2 and a family history of the condition. This number drops to 60 to 75 percent of people with no family history of the condition. There may be other genes or types of mutations causing this condition that doctors do not yet know about. Therefore, a person can still have neurofibromatosis type 2 even if no \( NF2 \) mutation is found.

**Prenatal genetic testing**

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known \( NF2 \) mutation in the family. Testing may take place either before pregnancy occurs or during pregnancy.
People considering prenatal testing should work with a genetic counselor to review the pros and cons of the testing. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

**Testing that occurs before pregnancy**—Testing that happens before pregnancy is called preimplantation genetic diagnosis (PGD). This special type of genetic testing is done along with in vitro fertilization (IVF). PGD offers a way to test embryos for a known NF2 mutation before placing them into the uterus.

**Testing that occurs during pregnancy**—Testing can be used to determine if a pregnancy is affected with a known NF2 mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)**—during the first trimester (first three months)
- **Amniocentesis**—during the second trimester or later (last six months)

Collected tissue can be checked for the presence of the NF2 mutation identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.

**Special concerns**

Genetic testing for neurofibromatosis type 2 is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the doctor or genetic counselor to be sure they understand the meaning of the results.

Sometimes children or adults with neurofibromatosis type 2 can feel sad, anxious or angry. Parents who pass on an NF2 mutation to one or more of their children can feel guilty. Some people with an NF2 mutation could have trouble getting disability coverage, life insurance or long-term care insurance in some states. More information about genetic discrimination can be found at [www.ginahelp.org](http://www.ginahelp.org).

**Are there other special health care needs for children with neurofibromatosis type 2?**

People of any age with neurofibromatosis type 2 have a higher risk of cancer. They should monitor their health and adopt healthful habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any cancer can be found early at the most treatable stage.
Other ideas to reduce the risk of cancer:

- Eat a healthful diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke

People with neurofibromatosis type 2 should watch closely for general signs or symptoms that could signal cancer, such as the following:

- Unexplained weight loss or fever
- Loss of appetite
- Aches, pains, lumps or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.

**What other information and resources are there for children with neurofibromatosis type 2 and their families?**

Resources about neurofibromatosis type 2:

- Neurofibromatosis Network ([www.nfnetwork.org](http://www.nfnetwork.org))
- Children’s Tumor Foundation ([www.ctf.org](http://www.ctf.org))

Other resources:


**Sources:**
1. Children’s Hospital of Philadelphia - Neurofibromatosis type 2 ([www.chop.edu/conditions-diseases/neurofibromatosis-type-2#.Va-wT2fbI5s](http://www.chop.edu/conditions-diseases/neurofibromatosis-type-2#.Va-wT2fbI5s))