

## Neurofibromatoses

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Neurofibromatoses (NF) are genetic disorders of the nervous system that result in the growth of noncancerous tumors along nerves. NF also can cause abnormalities of skin and bone.

There are two main forms of NF:

- NF1, formerly called peripheral neurofibromatosis or von Recklinghausen's disease
- NF2, formerly called bilateral acoustic neurofibromatosis, central neurofibromatosis or vestibular schwannoma

In both, severity of symptoms varies greatly. Many people thought that the deformities portrayed in the book, play and movie called *The Elephant Man* reflected an extreme case of NF1. Now, however, evidence indicates that the person portrayed had a different disorder called Proteus syndrome. Individuals with NF1 need not worry about becoming as disfigured as the Elephant Man.

### How common is NF?

NF1 is one of the most common genetic disorders. It affects about 1 in 3,000 births in the United States (1, 2). NF2 is less common, occurring in about 1 in 25,000 births (1, 2). Both forms of NF are found in every racial and ethnic group throughout the world and affect both sexes equally.

### What causes NF?

NF1 and NF2 are caused by abnormalities in two different genes. The gene for NF1 is located on chromosome 17, and the gene for NF2 is on chromosome 22. In about 50 percent of cases, the abnormal gene for either NF1 or NF2 is inherited from one parent who has the disorder. In some cases, the affected parent may have such mild symptoms that he or she may be unaware of having the disorder.

The remaining half of NF1 and NF2 cases are caused by new mutations (changes) in the causative genes (3). Thus, NF1 or NF2 can occur in a person who has no family history of the condition. The abnormal gene in each form of NF is autosomal dominant, so that any child of one parent with NF (the other parent is unaffected) has a 50-50 chance of inheriting the NF gene.

### What are the signs of NF1?

According to the National Institutes of Health (NIH), there are seven common signs of NF1 (4). NF1 is diagnosed in individuals who have two or more of these signs:

1. Six or more tan spots on the skin, called café-au-lait spots, that are wider than 1/5 inch before puberty or 3/5 inch after puberty. (In French, café-au-lait means "coffee with milk.") These spots are usually present at birth or appear by 2 years of age. Café-au-lait spots may increase in size and number and darken with age.
2. Freckles that appear under the arms or in the groin, usually by 7 years of age.
3. Two or more benign (noncancerous) tumors (lumps), called neurofibromas, under the skin or deeper. (A person may have a single neurofibroma without having NF.) Neurofibromas grow on nerves and are made up of cells that surround nerves and of certain other cell types. These tumors usually develop at around the time of puberty, but they may develop at any age. An

affected person may have any number of neurofibromas.

4. A tumor on the optic (eye) nerve, called an optic glioma. This tumor rarely impairs sight. Most of these tumors, which are usually diagnosed by 7 years of age, cause no symptoms and require no treatment.
5. Two or more tiny tan or brown Lisch nodules, which are small clumps of pigment that appear in the iris (colored part of the eye). These usually appear at around puberty and cause no vision problems.
6. A variety of bone defects, such as bowing of the legs below the knee. These usually are present at birth or develop during the first year of life.
7. A family history of NF1 in a parent, sibling or child.

### **How is NF1 diagnosed?**

NF1 is diagnosed by physical examination. The examiner may use a special lamp to check the skin, so that very light-colored café-au-lait spots can be noted. The examiner may recommend additional tests, including X-rays and other imaging tests [computerized tomography (CT scans) and magnetic resonance imaging (MRI)]. In some cases, genetic testing of a blood sample is needed to confirm the diagnosis.

Some children under 8 years of age may have café-au-lait spots, but no other signs of NF1. These children should be monitored carefully to see if other signs of the disorder develop.

### **How does NF1 affect a person?**

In many cases of NF1, symptoms are mild, and affected individuals live a normal life. Some characteristics of NF1, including café-au-lait spots, freckling and Lisch nodules, pose no risk to health. Some individuals have many skin neurofibromas on the face and body. Although skin neurofibromas are mainly of cosmetic concern, they can cause psychological distress.

Neurofibromas also can grow inside the body and can affect many organ systems. These deep neurofibromas (referred to as plexiform neurofibromas) affect about 30 percent of individuals with NF1 (1, 2). Some plexiform neurofibromas cause no symptoms, but others can result in serious problems, depending on the organ system involved.

Up to 60 percent of children with NF1 have learning disabilities (1, 5). Hyperactivity and problems with attention are common. Some affected children and adults have large heads, though this usually does not reflect a serious medical problem. Scoliosis (a progressive curvature of the spine) is common in NF1 and can begin at an early age. Short stature also is common. Eye tumors may cause bulging of the eye or visual difficulties. Less frequent complications include seizures and high blood pressure.

In about 3 percent of affected people, one or more fibromas become malignant and require treatment (surgery, chemotherapy and/or radiation therapy) (5). Individuals with NF1 appear to be at an increased risk of leukemia and certain rare cancers (5).

### **How is NF1 treated?**

There is no cure for NF1, but there are ways to treat some of its effects. Surgery can remove painful or disfiguring skin tumors. However, they often grow back. Optic gliomas that affect vision can be treated with surgery and/or radiation. Scoliosis may be treated by surgery or by wearing a brace.

A number of multidisciplinary NF clinics throughout the United States address specific medical concerns and routine NF-related health care issues.

### **How does NF1 affect pregnancy?**

Most women with NF1 have healthy pregnancies. However, neurofibromas may increase during pregnancy, apparently because of hormonal changes. This may sometimes contribute to pregnancy complications, such as compression of the umbilical cord or obstruction of the birth canal (requiring [cesarean section](#)) (1, 6). A pregnant woman with NF1 should be cared for by an obstetrician who is familiar with NF1, in close consultation with her NF specialist.

### **What are the signs of NF2?**

Almost all individuals with NF2 develop tumors that grow on the nerve from the ear to the brain, called the eighth cranial nerve (one of the 12 pairs of nerves that emerge from the brain.) These tumors are called schwannomas because they come from Schwann cells, which support and protect nerve cells. They often cause pressure on the acoustic (hearing) nerves, resulting in hearing loss. Many persons with NF2 also develop tumors on nerve tissues elsewhere in the body, including the brain and spinal cord. They also may develop a special type of cataract (clouding of the eye's lens) early in life. Persons with NF2 have few, or no, café-au-lait spots or neurofibromas, although they may have a small number of skin tumors (also called schwannomas).

### **How is NF2 diagnosed?**

As with NF1, NF2 usually is diagnosed by physical examination. The examiner may recommend a number of imaging tests, including MRI, to look at the brain and spinal cord. MRI can detect tiny tumors, allowing for early diagnosis. In some cases, genetic testing is done to help confirm the diagnosis.

When NF2 is diagnosed, hearing tests (audiometry and brainstem auditory evoked response test) are recommended to determine how well the eighth cranial nerve is functioning. The individual also should be examined by an ophthalmologist (eye specialist) to look for cataracts and other eye problems that can contribute to vision loss.

### **How does NF2 affect a person?**

Symptoms of NF2 usually appear in the teens or early twenties and include hearing loss, ringing in the ears, dizziness, facial numbness, balance problems and headaches (2).

Occasionally, spinal cord tumors can cause numbness or weakness in parts of the body, such as the legs. Some individuals may have weakness in one arm or leg if tumors grow in nerves in the armpit or groin. Cataracts can result in vision loss.

### **How is NF2 treated?**

As is the case in NF1, there is no cure for NF2, but surgery and radiation treatment can help control symptoms. MRI scans can detect very small tumors, sometimes allowing for early treatment. However, surgery on the eighth cranial nerve can sometimes result in additional hearing loss, so individuals and families must carefully weigh the risks and benefits of surgery. Sometimes removing part of a tumor, followed by radiation treatment, or radiation treatment alone, can help relieve symptoms.

### **Is genetic testing available to help diagnose NF1 and NF2?**

Yes. Genetic testing is available, and it can help confirm the diagnosis of NF1 and NF2. Genetic testing also can be conducted before birth and to help identify individuals with a family history of these disorders who do not yet show symptoms. However, genetic tests cannot predict the degree of severity of either form of NF.

[Genetic counseling](#) may be helpful to people with NF who are considering having children. Genetic counselors can explain the risks to offspring and discuss prenatal testing. Genetic counselors can be found at medical centers throughout the country.

### **Are there other forms of NF?**

Occasionally, cases of NF occur that are not consistent with NF1 or NF2. Less is known about these conditions, including their genetic causes.

One recently identified, uncommon form of NF is called schwannomatosis. Affected individuals develop schwannomas, as do many people with NF2. However, the schwannomas do not develop on the eighth cranial nerve, so affected individuals do not develop hearing loss. The main symptom of schwannomatosis is pain, which can occur in any part of the body. Affected individuals also may have some other neurological problems, such as numbness, tingling, or weakness in fingers and toes (4). Schwannomas often can be surgically removed to relieve pain (although tumors sometimes grow back).

### **Does the March of Dimes conduct research on NF?**

The March of Dimes has funded NF studies, including basic research on the causes of these and other nervous system diseases. For example, researchers are studying genetically controlled events in the embryo that are crucial to development of the body's nervous system and factors that regulate growth and maintenance of nerves.

### **For more information**

- [The Neurofibromatosis Information Page](#), The National Institute of Neurological Disorders and Stroke (NINDS)
- [The Children's Tumor Foundation](#)
- [Neurofibromatosis, Inc.](#)

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