



Neurofibromatosis, type 1 (NF1) is a genetic condition that can cause certain pigment (color) changes on the skin, an increased risk for certain types of cancer, and benign tumors in the skin, brain, and other parts of the body. The signs of NF1 can usually be found in childhood, and the first signs that are found are often the skin pigment changes, which can sometimes be very subtle. As people with NF1 get older, their chance to develop the tumors and cancer increase.

Individuals with NF1 can live normal lives, but they may develop serious health problems if they are not closely monitored by a healthcare provider who has experience with it. NF1 can potentially affect multiple body systems, and can affect individuals very differently. Individuals with NF1 are also at an increased risk to have scoliosis (curvature of the spine) or other bone abnormalities, as well as other tumors of the gastrointestinal tract or central nervous system. About half of people with NF1 also have learning disabilities.

### Causes

We have over 20,000 different genes in the body. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *NF1* gene makes a protein called neurofibromin. Neurofibromin works with other proteins to control how quickly the body's cells multiply (called a tumor suppressor protein). If someone has a harmful change (called a pathogenic variant) in one of their *NF1* genes, then their body does not make as much neurofibromin as it should. Without enough neurofibromin, there is not proper control over how fast our cells grow, which can lead them to multiply more cell growth than there should be. This unregulated cell growth can lead to tumors and the other signs and symptoms that we associate with NF1.

Pathogenic variants in the *NF1* gene cause NF1, and are inherited in an [autosomal dominant](#) pattern, meaning that children of a carrier each have a 50% risk to inherit the pathogenic variant and associated health risks. Notably, women and men both have the *NF1* genes and have the same chances to inherit and pass down variants in these genes. Therefore, both sides of the family are important when assessing inherited risk. About 50% (or 1 in 2 people) with NF1 will also have a parent with NF1. The other 50% have no family history and will be the first ones in their family with this condition.

It is estimated that approximately 1 in 3,000 people have NF1.



## Genetic Testing for NF1

Genetic testing for NF1 is not always needed, as it can be diagnosed via physical exam by a genetics specialist. There are some instances where genetic testing can be helpful:

- If someone is suspected to have NF1 but this is not confirmed by the physical exam
- If a child has a suspicious tumor, and genetic testing would immediately impact their treatment
- If a parent who has NF1 would like to do [prenatal](#) or [preconception testing](#) to determine if an embryo or pregnancy is also affected with NF1.

Genetic testing for pathogenic variants in *NF1* is currently available, but there are a few different ways to approach testing:

- [Single site analysis](#): Testing specific to a known pathogenic variant in the family
- Full gene [sequencing](#) and [rearrangement analysis](#): Comprehensive testing to search for all currently detectable pathogenic variants in the gene
- [Microarray](#) analysis to detect large deletions in the *NF1* gene
- [Gene panels](#): Newer, more broadly based gene tests that would include not only the *NF1* gene, but other genes known or suspected to be associated with the signs of NF1 or breast cancer. For example, pathogenic variants in the *SPRED1* gene can result in skin findings that can be similar to NF1, but does not have the increased risk for tumors and cancer that individuals with NF1 have. The *NF1* gene is also on some panels that are testing for an increased risk for breast cancer, along with genes such as [BRCA1](#) and [BRCA2](#).

## Diagnosing NF1

NF1 is diagnosed by detailed physical examination (usually done by a geneticist) and family history. The geneticist can look for the signs of NF1 during the examination and usually can determine if someone has NF1 or not based on that physical exam.

NF1 is suspected in a person with any of the following:

- Six or more cafe-au-lait (light brown spots)
- Two or more neurofibromas (a type of benign nerve tumor), or one plexiform neurofibroma (a more specific type of neurofibroma); neurofibromas can range from small, discrete lumps to larger internal masses
- Freckles in the groin or underarm area



- Optic glioma (benign tumors on the nerve that connects the eyes to the brain, which can sometimes affect vision)
- Two or more Lisch nodules (benign growths, like freckles, on the iris of the eye)
- A first-degree relative (parent, sibling, or child) with NF1
- Bone abnormalities, such as sphenoid dysplasia (abnormal bone at the base of the skull) and tibial pseudarthrosis (when the larger of the two bones in the lower leg breaks and does not heal correctly)

Individuals with NF1 also have an increased risk for specific types of cancer, scoliosis, and learning delays. Because the diagnosis of NF1 is made by a doctor's exam, genetic testing for NF1 is generally **not** recommended.

If you or your family meet any of the above criteria, a meeting with a pediatric or adult genetics specialist can be helpful to further determine if someone has NF1.

### **NF1 and cancer**

The overall lifetime risk for cancer in NF1 is approximately 60%, which includes an increased risk for breast cancer, and certain gastrointestinal and central nervous system cancers (such as [pheochromocytoma](#) and malignant peripheral nerve sheath tumors). Studies have shown that women with NF1 have an elevated risk to develop breast cancer before the age of 50. After age 50, the risk to develop breast cancer returns to the level of other women in the general population.

### **Medical Management for NF1**

Medical management for someone with NF1 and should be overseen by a medical provider who is familiar with NF1. Because NF1 affects people in very different ways, medical management should be specific to an individual's needs. The frequency of each screening tool is tailored to an individual's age. Some options for surveillance include:

- Regular eye exam
- Regular neurological exams and physicals
- Blood pressure monitoring
- MRI of the body and brain
- Breast cancer screening in women starting at age 30

The [National Comprehensive Cancer Network \(NCCN\)](#) recommends that women who have a diagnosis of NF1 should start annual mammogram screening at age 30, and should consider



annual breast MRIs between the ages of 30 and 50. It is important to note the possibility that benign neurofibromas within the breast tissue may cause false-positive results on MRI. There is not currently any data or evidence to recommend risk-reducing mastectomies for women with NF1, but it may be considered on a case-by-case basis depending on family history. More personalized recommendations will take into account your personal and family history, and should be discussed with your medical provider.

Click [here](#) to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.

Click [here](#) to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

**Additional Resources:**

[The Washington University Neurofibromatosis Center](#)

[Children's Tumor Foundation](#)

[Neurofibromatosis Network](#)