# Neurofibromatosis

The neurofibromatosis are genetic disorders of the nervous system. They mostly affect the development and growth of nerve (*neural*) cell tissues. These disorders cause tumors to grow on nerves. They can produce other abnormalities, too. They include skin changes and bone deformities. Scientists have classified the disorders as neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2). Of the two, NF1 is the more common type.

## CAUSES

Many affected persons inherit the disorder. But between 30 and 50 percent of new cases arise through change (*mutation*) in an individual's genes. Once this change has taken place, the mutant gene can be passed on to future generations.

## SYMPTOMS

Early symptoms may include:

- Ringing noise in the ear (*tinnitus*).
- Poor balance.

Problems caused by pressure from the tumors include:

- Headache.
- Facial pain or numbness.
- Symptoms of NF1, particularly those on the skin, are often evident at birth or during infancy. They almost always appear by the time a child is about 10 years old.
- NF2 has bilateral (occurring on both sides of the body) tumors on the eighth cranial nerve. The tumors cause pressure damage to neighboring nerves.

## DIAGNOSIS

In diagnosing NF1, a caregiver looks for:

- Changes in skin appearance.
- Tumors.
- Bone abnormalities.
- A parent, sibling, or child with NF1.

To diagnose NF2, a caregiver looks for:

- Bilateral eighth nerve tumors.
- Similar signs and symptoms in a parent, sibling, or child. Affected individuals may notice hearing loss as early as the teen years.

## TREATMENT

Treatments for both NF1 and NF2 are presently aimed at controlling symptoms.

- Surgery can help some NF1 bone malformations. It can remove painful or disfiguring tumors. But there is a chance that the tumors may grow back and in greater numbers. In the rare instances when tumors become malignant (3 to 5 percent of all cases), treatment may include surgery, radiation, or chemotherapy.
- For NF2, improved diagnostic technologies, such as MRI, can reveal tumors as small as a few millimeters in diameter. This allows for early treatment. Surgery to remove tumors completely is one option. But it may result in hearing loss. Other options include partial removal of tumors or radiation. If the tumors are not progressing rapidly, the conservative approach is watchful waiting.
- Genetic testing is available for families with documented cases of NF1 and NF2.
- New (spontaneous) mutations cannot be confirmed genetically.
- Prenatal diagnosis of familial NF1 or NF2 is also possible. Amniocentesis or chorionic villus sampling procedures would be used.

## WHAT WILL HAPPEN

In most cases, symptoms of NF1 are mild. So patients live normal and productive lives. But in some cases, NF1 can be severely debilitating. In some cases of NF2, the damage to nearby vital structures, such as other cranial

nerves and the brainstem, can be life-threatening.

## RESEARCH BEING DONE

- Several years ago, research teams located the exact position of the NF1 gene on chromosome 17. The product of the NF1 gene is a large and complex protein. It is called neurofibromin. One portion of this protein is similar to a family of proteins called GAP (guanosine triphosphatase-activating protein). Scientists have found that GAP proteins play a major role in tumor suppression in certain cancers. The similarity of the NF1 protein to GAP proteins suggests that the NF1 protein may have a similar switching role in the development of neurofibromas. Scientists theorize that defects in the gene may lessen or inhibit the normal output of its protein and allow the irregular cell growth that may lead to tumor development.
- The NF2 gene has been located on chromosome 22. The NF2 gene product is a tumor suppressor protein. Basic studies in molecular genetics may lead one day to nonsurgical or pharmacologic treatments. These would be aimed at suppressing tumors associated with the neurofibromatosis. The Medical Genetics Research Program at the NIH Clinical Center conducts NF2 family history research. Using specimens from some of the families, scientists have sequenced the NF2 gene. They have described two different patterns of clinical features in NF2 patients. Investigators are continuing to study these patterns. They want to see if they correspond to specific types of gene mutations.

**Research is continually being done to learn more about this problem.**
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