



Neurofibromatosis Type 2: Information for Patients & Families

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Neurofibromatosis Type 2 is a rare genetic disease, which causes nervous system tumors. We have written this pamphlet to give you some basic information about a complicated process. We hope you will use this information to ask more questions of your healthcare provider. We have tried, whenever possible, to include and explain medical terminology that you may encounter. A glossary of medical terms is included at the end of this pamphlet.

Neurofibromatosis Type 2 (also called bilateral acoustic neurofibromatosis or central neurofibromatosis and abbreviated as NF2, NF11 or BAN) affects about 1 in 40,000 people without regard to sex or race. Persons with NF2 are at a high risk for developing brain tumors and almost all affected individuals develop tumors on both nerves to the ears (also called the eighth cranial nerve). This nerve has two portions: the acoustic (hearing) nerve which carries information about sound to the brain and the vestibular nerve which carries balance information to the brain. The early symptoms of NF2 are symptoms of dysfunction of these nerves: hearing loss, ringing in the ears (called tinnitus) and problems with balance.

Although tumors on the eighth cranial nerve are most common, persons with NF2 can develop tumors on other nerves also. These tumors are called schwannomas because they arise from the Schwann cells. Schwann cells support and protect nerve cells and provide nerves with the insulation they need to conduct information. The symptoms of a schwannoma will depend on its location. Those that arise on cranial nerves (like the eighth cranial nerve tumors) affect the head and neck unless they grow large enough to push on the base of the brain (called the brainstem) and affect the body also. Those which grow on nerves as they exit the spinal cord may cause numbness of a part of the body; some tumors may grow large enough to press on the spinal cord and cause weakness and numbness in the legs. Those that grow in the bundles of nerves gathered in the armpits and groin area may cause weakness in one arm or leg. Schwannomas may even grow in tiny nerves in the skin where one can see them. These peripheral schwannomas rarely cause neurological symptoms, but they may rub on clothing or be cosmetically disfiguring.

In addition to schwannomas, persons with NF2 occasionally develop other sorts of tumors, which grow on the coverings of the brain and spinal cord. These tumors (called ependymomas and meningiomas) may cause many different kinds of neurological symptoms depending on their locations. As with schwannomas, a physician may detect signs of a tumor on a detailed neurological examination before a patient can detect symptoms in everyday life. Finally, some persons with NF2 develop a special sort of cataract, known as a juvenile posterior sublenticular opacity, or have other problems with the eyes. Since cataracts are likely to impair vision if not removed, it is important for all persons with NF2 to have a detailed eye exam by a specialist familiar with NF2.

The time course of NF2 varies from individual to individual. Most individuals with NF2 get their first symptoms during late teenage years or in their early 20's. A few people develop symptoms in

childhood and some do not have problems until their 40's or 50's. As mentioned above, the first symptoms are usually hearing loss, ringing in the ears or problems maintaining balance. A person will often have symptoms for many years before the true nature of the problem is realized. Since the tumors of NF2 grow slowly, it is likely that they are present in an individual for many years before they cause symptoms.

Presently the only treatments available for the tumors of NF2 are surgery and radiation therapy. Most persons with NF2 require at least one operation during their lifetime. Since the tumors of NF2 lie on nerves and/or near the brain and spinal cord, their surgical removal is not without risk. Surgery in these small and delicate areas may cause further injury to nerves—and further neurological problems. For these reasons, the risk of surgical damage should always be carefully weighted against the potential benefits of the proposed procedure. When surgery is no longer an option for a particular person because of their medical problems or the size or location of a tumor; radiation therapy may be considered. As with surgery, radiation therapy has both risks and benefits, which must be carefully considered.

Once someone has been found to have NF2, a number of tests may be helpful to define its nature and progression. The two most common tests are the MRI (magnetic resonance imaging) scan and audiometry (a hearing test). MRI scans are used to visualize the anatomy of the body. They are most commonly taken of the brain, but may also be used to "see" the spine or nerves in the arms and legs. To take an MRI scan a patient is asked to lie very still on a small bed which slides into a donut-shaped machine. Magnets are activated around the patient and produce a banging sound. At some point, the patient may be injected with a dye that enhances the appearance of some parts of the brain. No X-irradiation is used. Repeated MRI scans over time will define if a tumor is static or growing. This is important information since a large static tumor may cause fewer problems than a small but growing tumor.

Although MRI scans can show very detailed structural information (what your body looks like), they cannot show functional information (how well your body is working). Audiometry tests how well the hearing portion of the eighth cranial nerve is working. To undergo audiometry a person puts on earphones in a soundproof room. Sounds of different intensity and pitch are given to each ear and the ability to detect them is monitored. Information from audiometry augments the structural information from an MRI. Repeated audiometry will determine if the functional aspects of a tumor are changing.

NF2 is a genetic disease that is passed from parent to child at the time of conception. About one half of persons with NF2 do not have a parent with the disorder and represent new genetic changes. All persons with NF2—those with affected parents and those without—have a 50-50 risk that each one of their children will be affected. Disorders such as NF2, which affect both sexes equally and are passed from an affected person to 50% of their children, are termed autosomal dominant disorders. The exact piece of genetic material which causes NF2 was identified on chromosome 22. This identification often makes it possible to find, by a blood test, if a relative of a person with NF2 also has NF2. Just like surgery, this sort of genetic testing has both risks and benefits and should be discussed thoroughly with your healthcare provider.

The information in this pamphlet is meant to be an introduction to a very complicated disease. We hope that this information provides a groundwork for you and your family to understand this disease better and allows you to ask informed questions of your healthcare provider. If you or a relative has NF2 you will need lifelong contact with a healthcare provider; and will probably have contact with multiple care providers including neurologists, surgeons and radiologists. We also encourage you to seek out peer support groups that may provide practical advice and support to augment professional providers' skills.

Some frequently asked questions about Neurofibromatosis Type 2

Q. What are the chances of: a boy having NF2 if his mother does? a boy having NF2 if his father does? a boy having NF2 if two sisters and one parent do?

A. The chances of a child having NF2 if a parent has NF2 are 50-50, regardless of sex or who else in the family is affected.

Q. If a person has NF2 what are the chances that one of her parents has NF2?

A. About half of persons with NF2 are new genetic alterations, and have no family history of the disease, thus if a person has NF2 chances are only 50-50 that one of her parents has the disease.

Q. If a person has NF2 but no one else in her family has NF2 what are the chances that her child will be affected?

A. 50-50. Although new genetic alterations are common in NF2, they do not alter the risk of passing along the gene.

Q. What is the most common problem that people with NF2 have? What are other problems that people with NF2 have?

A. The most common clinical problems are tinnitus (ringing in the ears), hearing loss and balance dysfunction. Anatomically, the most common problem is tumors on the nerve to the ear (the eighth cranial nerve), also known as vestibular schwannoma or acoustic neuroma. Other less common problems include spinal tumors, skin tumors, and cataracts.

Q. Do all people with NF2 become deaf? When a person with NF2 loses his hearing does it occur suddenly or gradually?

A. No, some people with NF2 retain hearing, especially on one side. Hearing loss may occur gradually over months or years, or suddenly over a day or week.

Q. Do people with NF2 ever develop NF1?

A. No. The two diseases are genetically and functionally distinct.

Q. If a person with NF2 has a brain tumor, what is the most common form of treatment? Are all NF2 associated brain tumors immediately treated?

A. The most common treatment for NF2 associated tumors is surgery. Other forms of treatment include hearing augmentation with mechanical aids and radiation therapy, including gamma knife therapy. Not all NF2 associated tumors are treated as soon as they are detected because many are quite slow growing and may remain for years without causing significant problems. Since treatment may cause neurological damage on its own, it is often more prudent to learn the natural history of a tumor before operating on it.

Q. How are the tumors of NF2 different from cancer?

A. The tumors of NF2 are different from cancer because they are slow growing and do not spread to other areas of the body.

Q. Can NF2 be cured?

A. No, NF2 cannot be cured at this time.

Q. What medical tests are important for people with NF2 to have? Is there a blood test for NF2?

A. The most important tests are brain imaging (magnetic resonance imaging) and audiometry (hearing tests). Other important tests are neurological exams, ophthalmologic exams and spinal imaging. There is a commercially available blood test for NF2 that may often be used in determining if a relative of a person with NF2 also has NF2. Because there are many personal, familial and social issues surrounding such genetic testing, it is best done in conjunction with a qualified genetic services provider.

Some unanswered questions about NF2

Q. Does X-ray exposure influence the course of NF2?

A. Although individual experiences suggest that X-ray exposure may increase the number of NF2 associated tumors, there have been no well-controlled studies of the issue.

Q. Do people with NF2 have an increased incidence of cancer?

A. The vast majority of tumors affecting NF2 patients are benign. If there is an association between NF2 and cancerous tumors it is certainly not striking.

Q. What is the probability that a person with NF2 will need an operation?

A. Since there is great variability in the course of NF2 between individuals and even in different times within the same person's life, it is very difficult to predict the probability of any single individual needing surgery. The vast majority of individuals with NF2 require surgery at some point in their life.

Q. Do people with NF2 become "senile" more often than those without the disease?

A. There is no evidence that individuals with NF2 become "senile" more often than the general population, but this has not been carefully studied.

Q. If I have NF2 will I die at a young age because of this disorder?

A. In past studies, the average life span of individuals with NF2 was considerably shortened compared to people without NF2. With improvements in diagnosis, monitoring and surgical techniques these data may not be applicable to individuals living now.

Q. Do prenatal factors cause or influence the course of NF2?

A. There is evidence that exposure of the father to toxic chemicals before conception may increase the incidence of new cases of NF1 and other tumors. This has not been looked at for NF2. In utero exposures would not be expected to alter the probability that an infant would be born with NF2, but is unknown if they may alter the course if the fetus is already affected with NF2.

Q. If a child is at risk for NF2, at what age should MRI scanning begin and at what age can it safely be stopped?

A. Since the average age of onset of symptoms in NF2 is late teens and early twenties, scanning has traditionally begun at that time. It is not clear if earlier studies would be beneficial. It is also not known at what age monitoring can safely be stopped. Although there are NF2 affected individuals who do not have symptoms until their 50's, it is possible that "silent" tumors would always be seen on an MRI scan earlier

Q. What effects do puberty, pregnancy, and menopause have on the tumors of NF2?

A. One of the tumor types associated with NF2 (the meningioma) is known to frequently be responsive to female hormones in its nongenetic form. There are also individual reports of acceleration of tumor growth in women with NF2 during exposures to female hormones. However, in the largest study to date of women with NF2, no significant changes were seen in the patients or their tumors during 100 individual pregnancies.

Glossary of medical terms

Audiometry—Functional testing of a person's hearing done by exposing each individual ear to various sounds in a soundproof room.

Autosomal dominant—Pattern of inheritance in which one half of an affected person's children are also affected without regards to sex of the child or parent. Autosomal refers to the fact that the genetic information for the disease lies on a non-sex chromosome. Dominant refers to the fact that only one piece of genetic information (out of the two which are received at conception) need be affected by the disease.

Cancer—An abnormal and uncontrolled growth of cells which invades the surrounding tissues, spreads to other parts of the body, and recurs and causes death if not completely treated.

Cataract—A clouding of the lens of the eye. If not treated, cataracts may cause blindness by blocking light rays from entering the eye.

Chromosome—String of genetic information carried by the cells of the body. Each person receives 22 non-sex chromosomes and 1 sex chromosome from each parent at conception. As the body grows, a complete set of these 46 chromosomes is replicated and placed in every cell of the body.

Ependymoma—Tumors which grows from cells which line the cavities of the brain and spinal cord.

Gamma knife —Form of highly focused radiation therapy.

Gene—Individual piece of genetic information. Genes are strung like beads in a predefined order on the chromosomes, Since each person has two copies of each chromosome, one from each parent, they also have two copies of each gene,

Magnetic Resonance Imaging—Method of visualizing the internal structures of the body by exposing the tissues to magnetic fields and measuring their response. MRI produces highly detailed pictures of the anatomy of the body and is especially useful for visualizing the brain. MRI produces no functional information on the area scanned.

Meningioma—Tumor which grows from the cells which line the brain and spinal cord in protective sheets called meninges.

Radiation therapy—Form of treatment in which the tumor cells are exposed to controlled doses of X-ray irradiation. Although tumor cells are especially susceptible to irradiation, surrounding

tissues will also be damaged. Radiation therapy rarely cures a tumor by itself, but may be a useful tool when used in conjunction with other forms of therapy, or when a patient can no longer tolerate other forms of therapy.

Schwannoma—Tumor which grows from cells which line the nerves of the body. These cells, called Schwann cells, not only protect the nerves but also provide them with the insulation they need to conduct electrical impulses to and from the brain.

Tinnitus—Ringing in the ears.

Tumor—An abnormal growth of cells. Tumors may be malignant in which case they are called cancers. Non-malignant tumors (benign) do not aggressively invade surrounding tissues or spread to other parts of the body, but they may cause significant symptoms and even death depending on their location.

ADDITIONAL INFORMATION

The Children's Tumor Foundation can be a source of educational materials and support. They can be reached at:

The Children's Tumor Foundation
95 Pine Street, 16th Floor
New York, NY 10005
212-344-6633 or 1-800-323-7938
Email: Info@ctf.org
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