

3rd Edition

Understanding Neurofibromatosis



AN INTRODUCTION FOR PATIENTS
AND PARENTS

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Understanding Neurofibromatosis:

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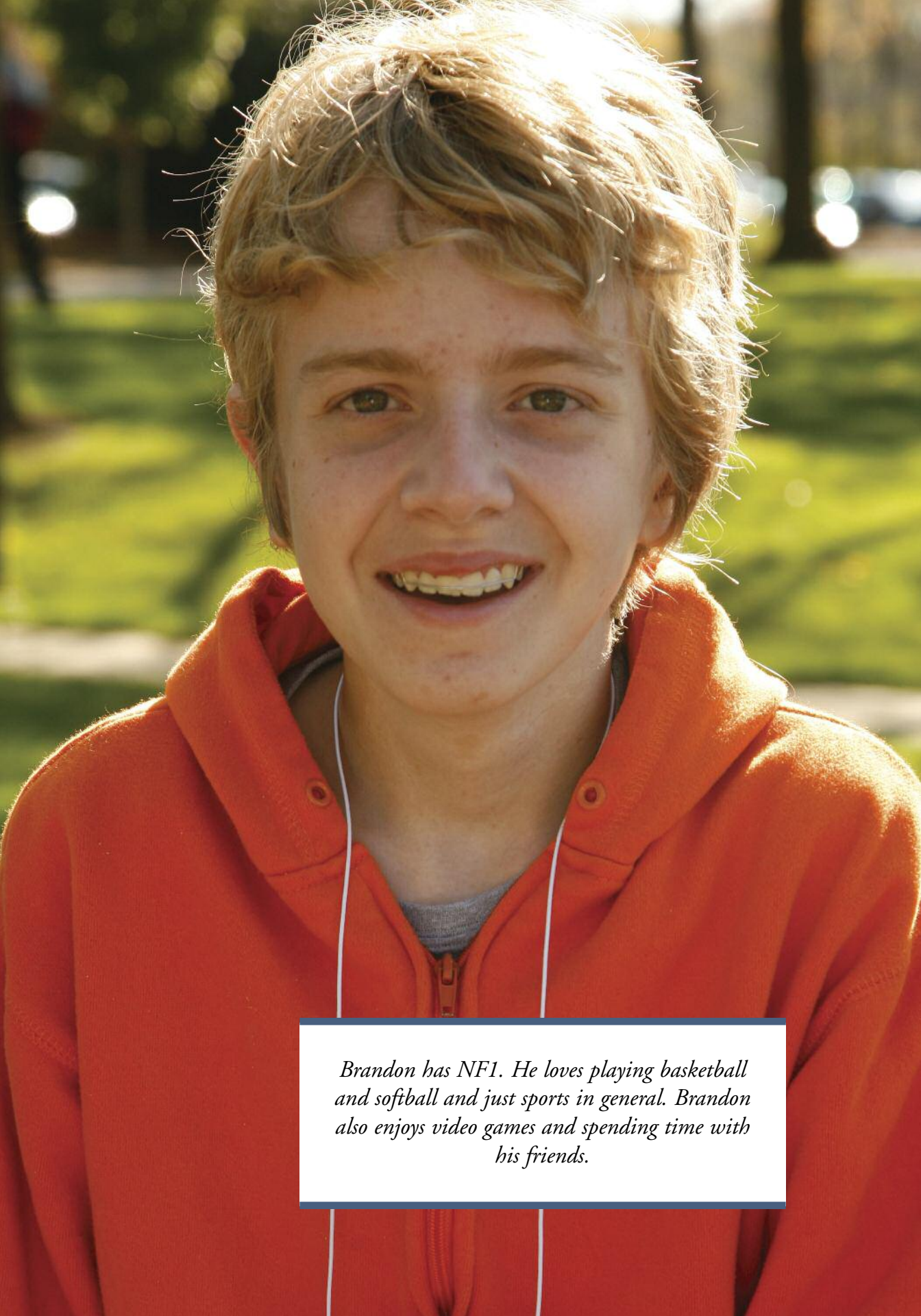
Dedicated to Peter Cooper

*Whose undaunted courage, resolute
determination, and great kindness
continue to inspire so many.*

*Neurofibromatosis Program
The University of Chicago Hospitals and Clinics*

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Brandon has NF1. He loves playing basketball and softball and just sports in general. Brandon also enjoys video games and spending time with his friends.

Understanding Neurofibromatosis

AN INTRODUCTION FOR PATIENTS AND PARENTS

Where To Begin?

This information is for families who have recently been told that one member may have Neurofibromatosis (NF). When you were first told about NF, you may only have heard the word Neurofibromatosis and nothing else. As some of the initial shock wears off, you will want to know more about this disorder or group of disorders because NF really is more than a single disorder. This booklet will explain what NF is, what causes NF, what your family will need to do about it, and who can help you.

What Is NF?

Neurofibromatosis (NF) is a genetic disorder that causes growths or tumors to form on nerves. These can occur anywhere in the body. NF is one of the most common genetic disorders. It occurs in every racial and ethnic group and affects both sexes equally. There are at least 100,000 people with NF in the United States. One in every 3,000 babies born has NF. Even though NF is relatively common, not many people have heard of it.

NF is one of the most common genetic disorders. It occurs in both sexes and every racial and ethnic group.

What Causes NF?

Neurofibromatosis (NF) is actually the name for at least two or three separate *genetic* disorders that can affect the nervous system as well as a number of other parts of the body. A genetic disorder is caused by an abnormal gene in your body. NF is not contagious.

There are six major concepts that will help you understand how the two kinds of NF are caused and how NF is passed on from parents to children:

1. Genes are inherited material in a cell that determine how the cell functions.
2. NF is caused by an abnormal gene.
3. NF can be due to a spontaneous change in a gene, or a person may inherit an abnormal gene.
4. If one of the parents has NF, there is a 50% chance that with each pregnancy the child will also have NF.
5. NF1 and NF2 are separate disorders resulting from changes in different genes. You usually cannot have both NF1 and NF2.
6. A third disorder, Schwannomatosis has some overlap with NF2.

That means you can't catch it from other people. However, a parent with NF may pass on the disorder to his/her children.

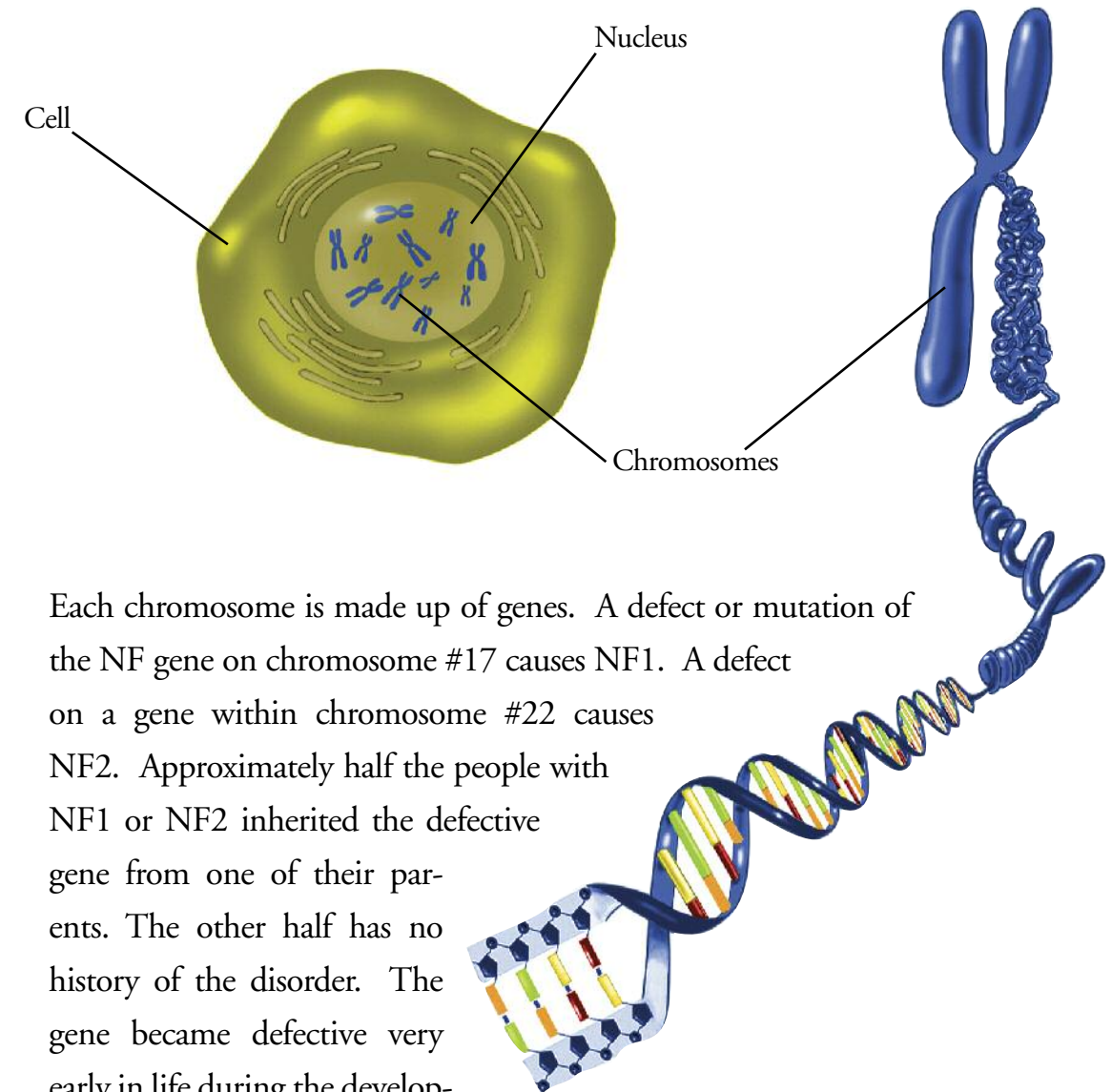
It is important to understand the two ways children are born with NF: (1) You can inherit an abnormal gene that causes NF from one of your parents, or (2) something can go wrong in one of your genes before birth. This second way of getting NF is called spontaneous gene mutation. If you have spontaneous gene mutation, you did not inherit NF, but you can pass it on to your children.

NF1 and NF2 are separate disorders because two different genes are affected. NF1 is caused by a change in a gene on chromosome 17. NF2 is caused by a change in a gene on chromosome 22. Because NF1 and NF2 are caused by changes in different genes, NF1 and NF2 very rarely occur in the same family.

Schwannomatosis appears to be due to changes in chromosome 22 and shares some features of NF2.

***Genetic:** inherited or basic, related to information contained on genes*

Our cells have 46 chromosomes. 23 come from the father and 23 from the mother, so there are 23 chromosomal pairs. The first 22 are numbered 1 to 22. The last pair are our sex chromosomes.



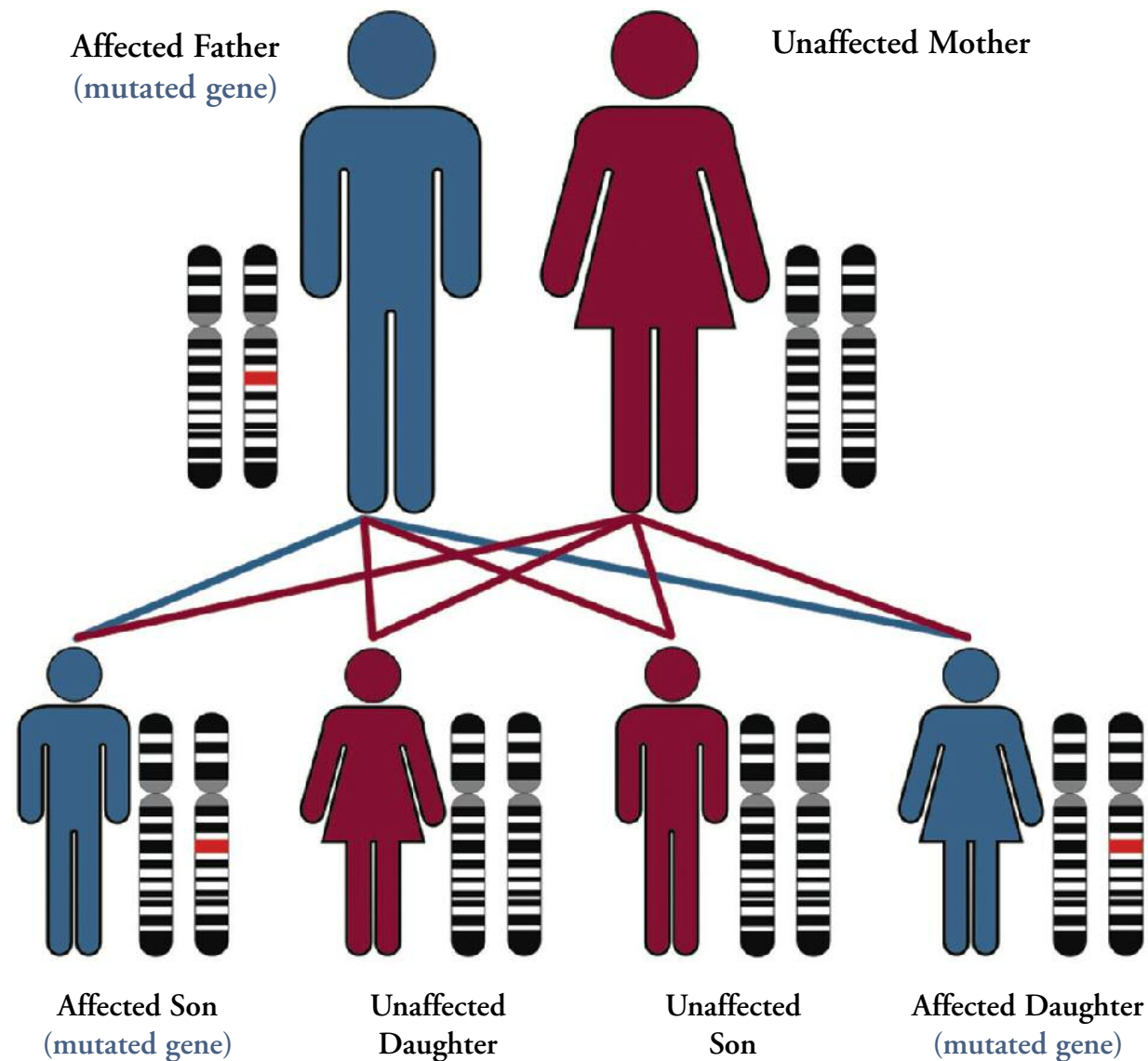
Each chromosome is made up of genes. A defect or mutation of the NF gene on chromosome #17 causes NF1. A defect on a gene within chromosome #22 causes NF2. Approximately half the people with NF1 or NF2 inherited the defective gene from one of their parents. The other half has no history of the disorder. The gene became defective very early in life during the development of the embryo.

Note: Since NF1 and NF2 are on different chromosomes they are different though similar disorders. For this reason it is highly unlikely to have both NF1 and NF2.

Autosomal Dominant Inheritance

The NF gene is a dominant gene. Anyone with the gene has the disorder.

Each child always receives a normal copy of the gene from the unaffected parent and either a normal or faulty gene from the affected parent.



If you have NF, you have a 50% chance of passing NF on to any child you have.

About NF1

The most common form of Neurofibromatosis (NF) is NF1, sometimes referred to as von Recklinghausen's disease. People with NF1 generally have brown oval or circular spots on the skin called *café-au-lait spots* and freckles under the arm or in the groin area. *Benign* soft tumors or lumps in or under the skin called *neurofibromas* and brownish-red spots in the iris, (the colored part of the eye), called *Lisch nodules* are present in most people.

NF1 frequently causes learning difficulties. It may affect physical growth and coordination. Tumors may form along nerves anywhere in the body.

Some signs of NF1 are usually visible within the first year of life.

Other signs of NF1 may develop as people get older. For example,

Lisch nodules of the iris develop in teenagers and adults. Neurofibromas frequently appear or grow during teenage and adult years. While problems caused by NF1 can be serious, NF1 usually does not keep people who have it from living productive lives.

Some people with NF1 will only have café-au-lait spots and neurofibromas, but others may have more difficult problems. At the present time, it is impossible to predict what kinds of problems an individual will have. No two people will be affected exactly the same way, even within the same family. However, as we learn more about the different gene changes that cause NF, we may be able to use gene testing to help us understand what problems patients may have.

NF1 can cause café-au-lait spots, benign tumors of the skin, or tumors below the skin affecting internal organs. Some people will have only mild problems while other people will be more severely affected. NF1 affects people differently, even within the same family.

Café-au-lait spots: brown oval spots on the skin the color of coffee with milk

Benign: not malignant or not cancer

Neurofibroma: Soft tumor in or under the skin

Lisch nodules: spots on the iris, the colored part of the eye. These do not interfere with vision

Specific Effects of NF1

While NF1 can affect almost any organ in the body, many people have only a few difficulties.

People with NF1 usually have normal intelligence, but as many as 60 percent of children have short attention span, hyperactivity, or learning disabilities. Problems with visual perception are common and may make spelling and math difficult. Other children can struggle with sounding out words, making it harder for them to learn to read. Problems with organization, impulse control and socialization are frequent. Children with these problems can be helped to be successful in school. Headaches and hearing issues are also common and may affect schoolwork.

NF1 frequently affects growth. People may be shorter or have slightly larger heads than average. NF1 may also affect the growth of bones. Some will have shrinkage of bone called *atrophy*, bending or fracture of a long bone that won't heal called *pseudarthrosis*, or curvature of the spine called *scoliosis*.

NF1 also causes tumors to form in different parts of the body. Small tumors on or below the surface of the skin, called neurofibromas, are present in most people.

Some people have tumors or growths that involve the skin and deeper tissues, including the nerves, called *plexiform neurofibromas*. These growths can sometimes be large and change the normal shape of a part of the body or can affect internal organs. Occasionally, cancer can form in a plexiform neurofibroma.

NF1 may also affect the brain. *Bright spots* are frequently seen on brain scans in young children. The nerves to the eye may be abnormally large, called *optic glioma*. In a small number of people, NF1 causes brain tumors.

Having NF1 means that there will be changes in your body that nobody can predict. Because doctors cannot tell in advance what will happen to each person, and many of the problems are rare, it is important for you to learn all that you can about NF1.

Atrophy: *shrinking or decrease in size*

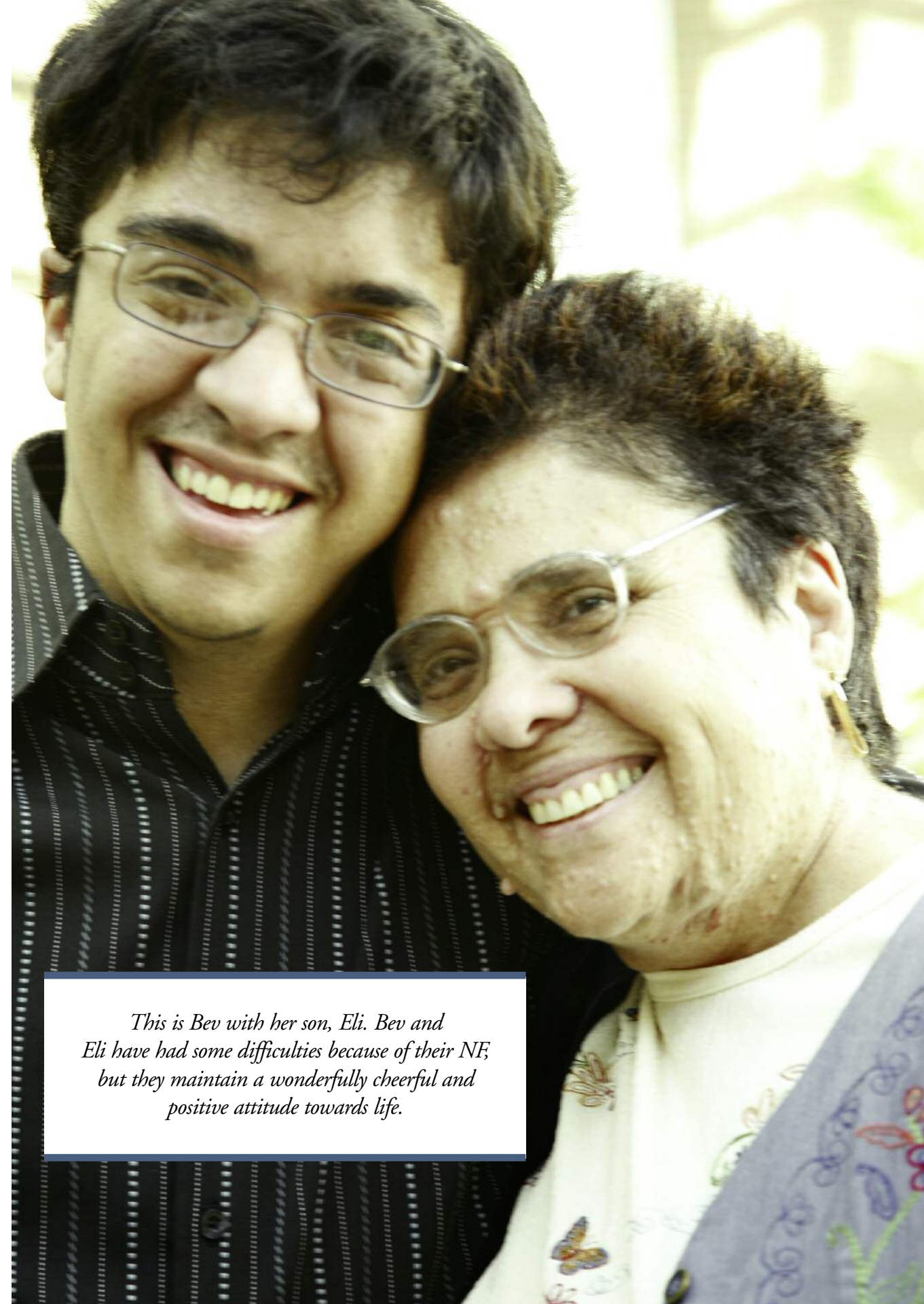
Pseudarthrosis: *fracture of a long bone that won't heal*

Scoliosis: *curvature of the spine*

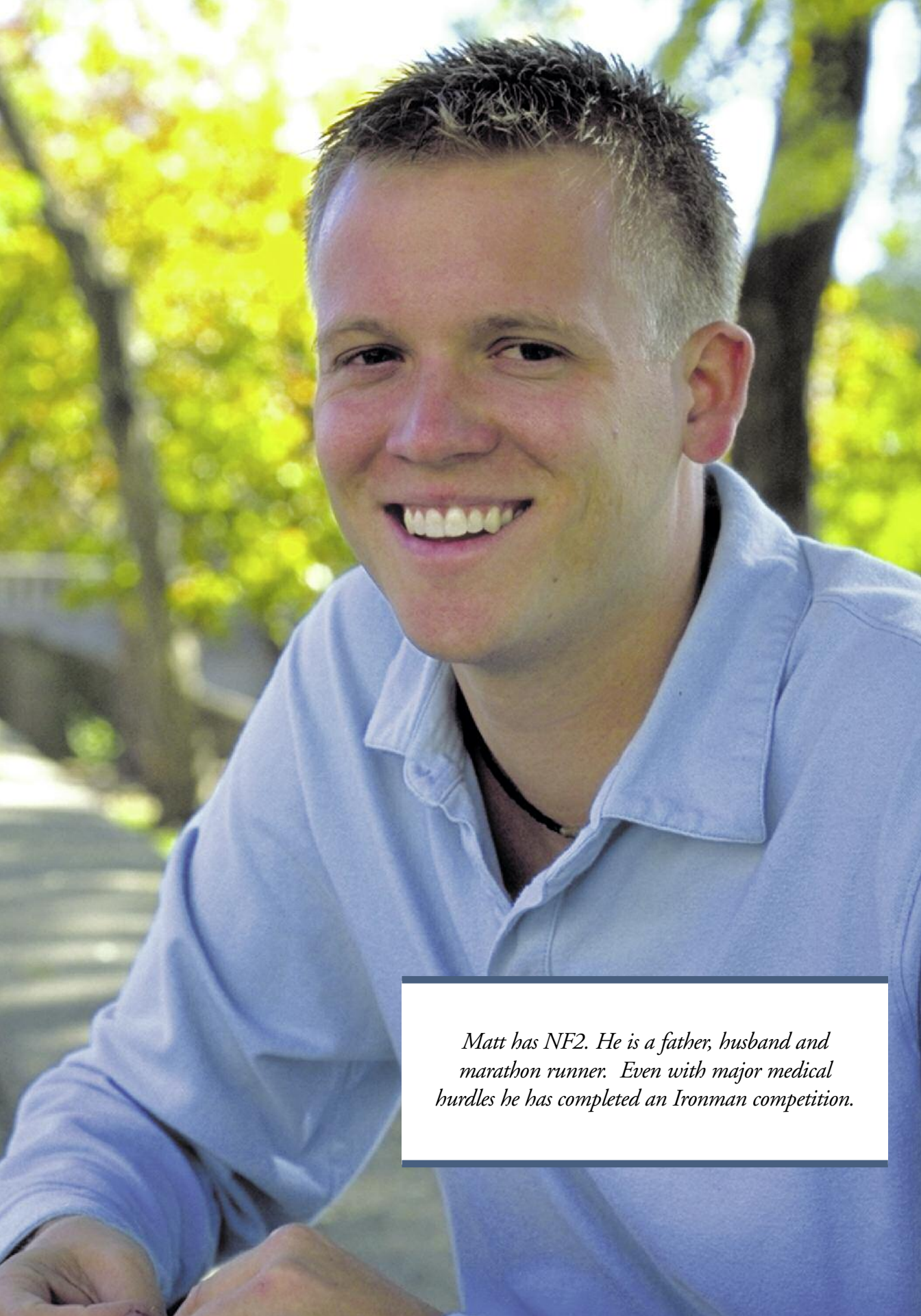
Plexiform neurofibroma: *diffuse tumor of the skin or deeper tissues*

Bright Spots: *spots found on MR scans that aren't brain tumors*

Optic glioma: *a growth on the nerve to the eye*



This is Bev with her son, Eli. Bev and Eli have had some difficulties because of their NF, but they maintain a wonderfully cheerful and positive attitude towards life.



Matt has NF2. He is a father, husband and marathon runner. Even with major medical hurdles he has completed an Ironman competition.

About NF2

NF2 is sometimes referred to as bilateral acoustic neuroma disease. Because it affects nerves next to the brain or spinal cord, the problems of NF2 can cause serious disabilities. Even so, many people with NF2 can lead relatively normal, rewarding lives and learn to compensate for deficits they may have.

In some, signs of NF2 are detectable in childhood, but for the majority, it is not apparent until late teenage or adult years. People with NF2 may only have a few *café-au-lait spots* on the skin. Skin tumors are few in number and can be easily overlooked. However, everyone with NF2 has tumors affecting hearing and balance (*vestibular schwannomas, previously called acoustic neuromas*).

Cataracts in the lens or changes in the retina of the eye are present in most people. Tumors that push on the brain or spinal cord (*meningiomas and schwannomas*), tumors along the peripheral nerves (*schwannomas*),

NF2 is a completely separate genetic disorder from NF1. NF2 causes tumors on the nerves for hearing and balance. NF2 is very different from NF1 both in its effects on the body and when it first appears.

or tumors within the spinal cord (*ependymomas*) occur in many people. These problems are serious because they can cause weakness or seizures, however, the tumors are *benign*.

While the problems in NF2 can be frightening, there have been important advances in treatment, detection, and understanding that offer considerable hope.

About Other Forms of NF Including Schwannomatosis

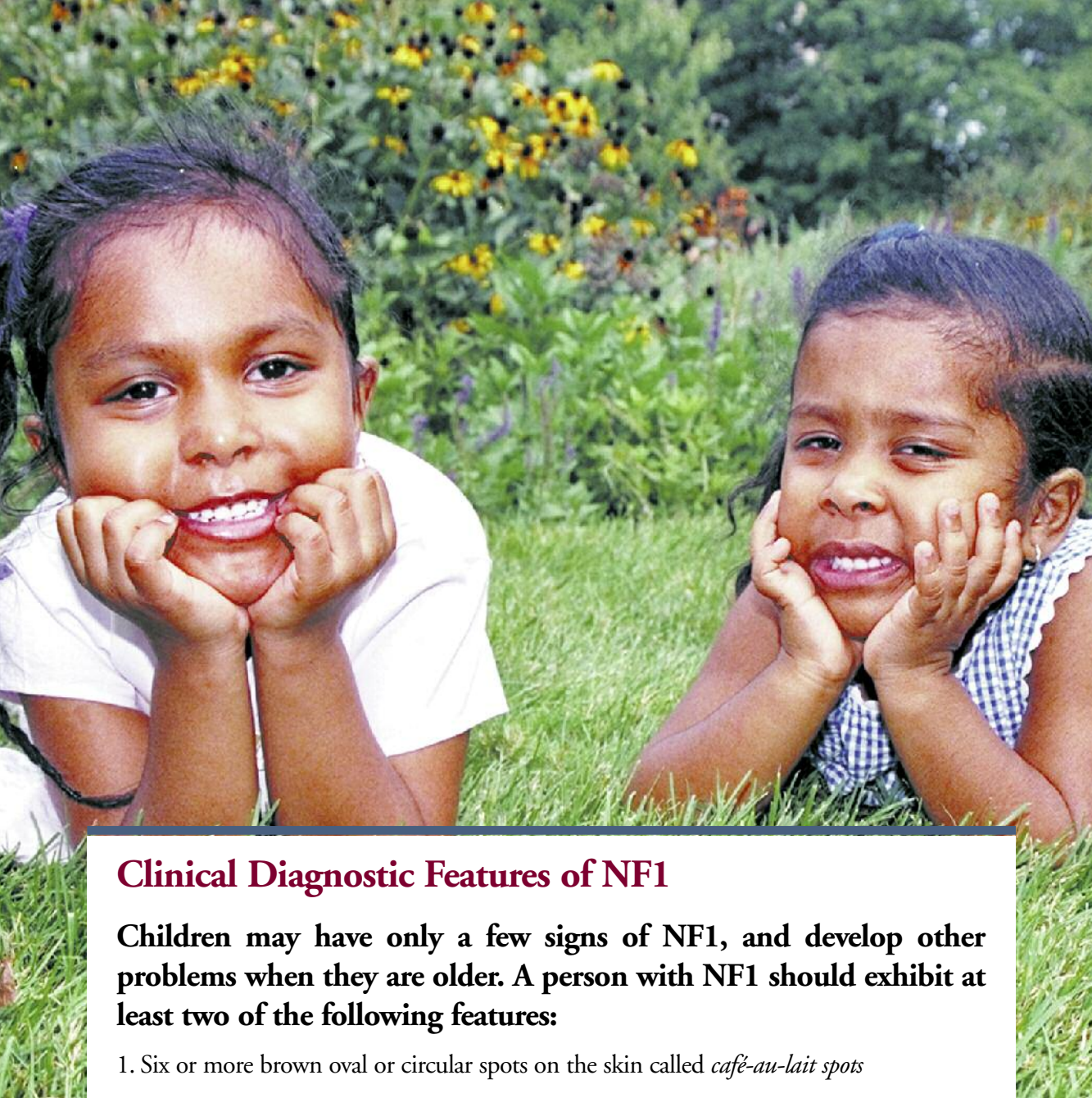
There are people who do not fit easily into a NF1 or NF2 category, or people in whom the signs of NF are located on only one side of the body. Additionally, people may have multiple tumors along nerves called schwannomas and pain without any other problems. These patients have a form of NF called Schwannomatosis. There is some overlap between NF2 and Schwannomatosis. Genetic testing can be helpful in identifying these uncommon forms of NF.

Vestibular, acoustic: the nerves for balance and hearing

Schwannomas, meningiomas: benign tumors of the nerves or brain

Benign: not malignant, not cancer

Cataract: A clouding of the eye lens that blocks light rays from entering the eye



Clinical Diagnostic Features of NF1

Children may have only a few signs of NF1, and develop other problems when they are older. A person with NF1 should exhibit at least two of the following features:

1. Six or more brown oval or circular spots on the skin called *café-au-lait spots*
2. Two or more benign skin tumors called *neurofibromas*, or one diffuse tumor of the soft tissue or nerves called a *plexiform neurofibroma*
3. Freckles under the arm or in the groin region
4. A tumor of the nerve to the eye called an *optic glioma*
5. Two or more spots on the iris called *Lisch nodules*
6. A problem of one of the bones such as bowing of a leg with or without a fracture
7. A parent, brother, sister, or child with NF1

How Do I Know that I or My Child Has Neurofibromatosis?

When someone is told that they or their child may have NF, one of the first questions is: How can you be sure? How do I know I have NF?

There is a blood test for NF1 and NF2. MRI's are also essential for the diagnosis of NF2.

The diagnosis of NF is usually made clinically on the basis of a careful

physical exam by a doctor who is familiar with NF.

Knowledge of NF is the best tool you and your doctors have in treating the disorder. A good first step is making sure you understand how a diagnosis of NF1 or NF2 is made. The **National Institute of Health** offers the following guidelines (see below).

Clinical Diagnostic Features of NF2

Signs of NF2 are not usually present until the teenage years or older. A person with NF2 should have:

1. Tumors of the *vestibular nerve* on both sides of the head
- OR**
2. A single *vestibular nerve tumor* before age 30 and a mother, father, brother, or sister with NF2
- OR**
3. A single vestibular schwannoma before age 30 and 2 of the following: *neurofibroma, meningioma, ependymoma, schwannoma, or juvenile cataract*
- OR**
4. Multiple *meningiomas* plus a single *vestibular schwannoma* or two of the following: *schwannoma, ependymoma, neurofibroma, juvenile cataract.*
-



Children with NF can have some problems learning but they can do well, either with the help of medication and/or educational programs directed to their needs.

After Neurofibromatosis Diagnosis:

What Do You Need to Do?

Identification of the genes for NF1 and NF2, offers tremendous hope for the future. For instance, identifying the NF1 gene has helped us understand how tumors in NF1 form. As we understand more about the gene, we hope to predict and control the problems caused by the abnormal gene.

While there is currently no cure for NF, there are many things you can do that will make a significant difference in your life or the lives of your children.

Remember, if your child has NF, you are your child's protector. If you, yourself, are affected, you must be your own advocate as well. This means that you must be sure you talk to your doctor about any new problems or concerns.

There are also many professionals besides your doctor you can rely on for help with NF. They include members of your local NF support group, genetic counselors, teachers, and psychologists.

Learn About NF

Because many of the problems associated with NF are rare, even among people with NF, most doctors will not have had enough experience with NF to detect or successfully treat each symptom. Successful treatment often depends on having a collaborative relationship between your local physician and other physicians in NF programs at major medical centers.

The best treatment also depends on your learning about NF so you can understand what problems you may expect and bring them to the attention of your doctors. If you notice changes, call your doctor and ask whether the change is associated with NF. It is often much easier to treat the NF related problems that occur if they are detected early.

Talk to your doctor about your problems and concerns. Write questions down. Make sure your doctor answers them and that you understand the answers.

Working with Your Doctors

It is important to get the advice of a doctor who treats many patients with NF. Don't hesitate to ask your doctor about his or her experience with NF. Do not be afraid to ask for a second opinion. Your family doctor should be willing to call an NF clinic to ask for advice. You may also want to consult an NF clinic in a medical center on your own for advice. Doctors at an NF clinic can then work with your family doctor to provide you with the best care.

Once NF has been diagnosed, it is important to begin a careful, organized program to spot any changes that may be due to NF and to keep good

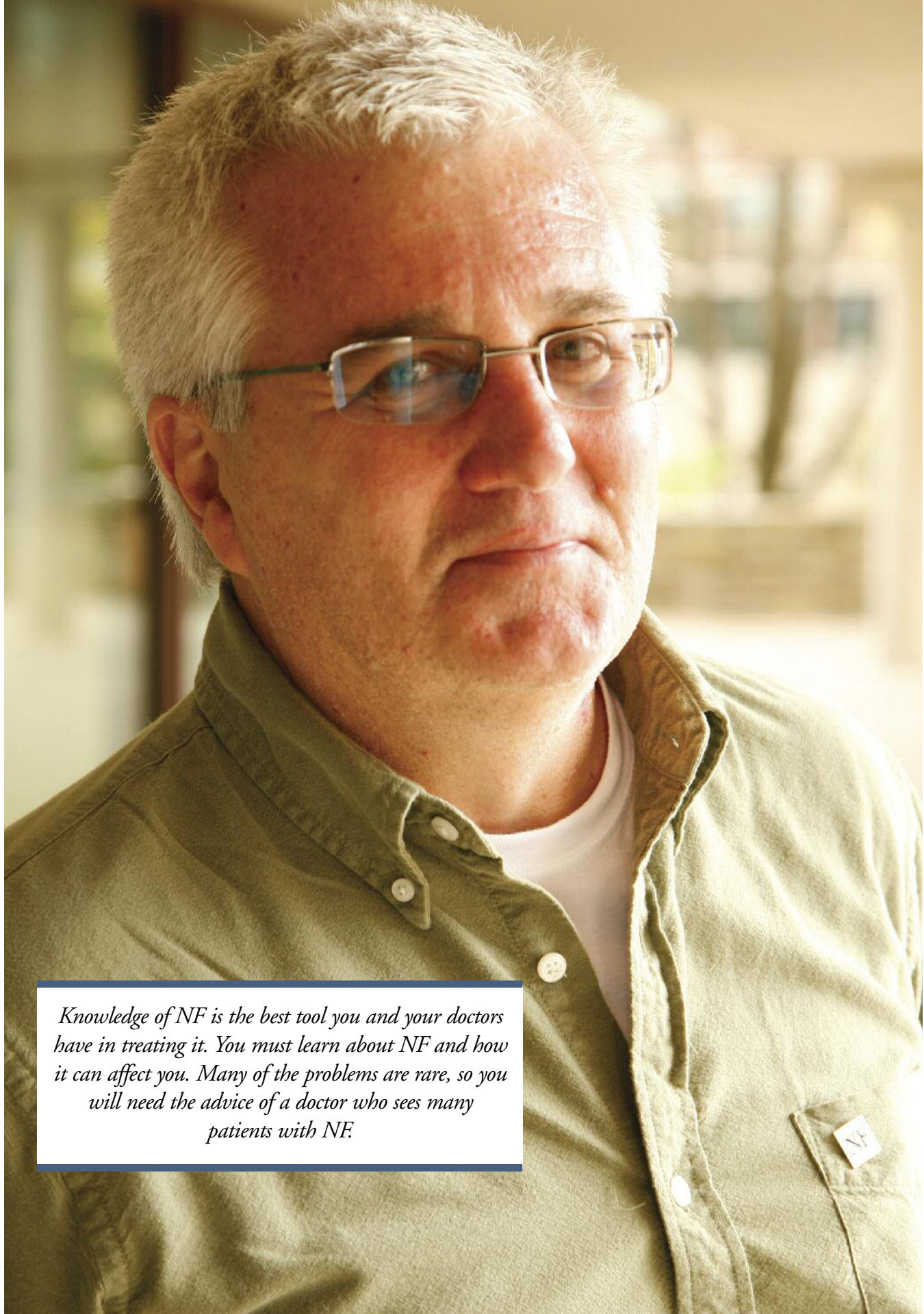
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1. Be aware of any changes that may be due to NF.
 2. Make regular doctor visits.
 3. Keep good medical records.
 4. Be cautious about information on the internet about NF. Many of the complications are quite rare. In addition, complications of NF1 are age specific. Neither the timing of complications or their frequency is explained on the internet.
-

records about these changes. Ask doctors for a copy of the examination report to keep for your own records. You may also want to keep copies of your x-rays or scans so you can discuss them with different doctors. Make regular doctor visits part of your routine.

Talk about your concerns with your friends and family or other people with NF.

Evaluate Your Family

It is important to know whether other people in your immediate family have NF. Identifying who in a family is affected may be a sensitive and difficult issue since guilt or shame are often associated with having a genetic disorder. However, there are good reasons for knowing who has NF. For example, if you have NF, then any of your children can have NF. However, if your child has NF and you are sure that neither of the parents is affected, then the chance of having another child with NF is very small.



Knowledge of NF is the best tool you and your doctors have in treating it. You must learn about NF and how it can affect you. Many of the problems are rare, so you will need the advice of a doctor who sees many patients with NF.

A careful physical examination, is the best way to determine if someone has NF, although blood tests for NF1, NF2 and Schwannomatosis can be very helpful. Sometimes it is also necessary to do genetic testing on tumor samples to evaluate NF2 or Schwannomatosis. You can use this information to plan a family. You may want to discuss this with your doctor or a genetic counselor. Genetic counselors are trained to provide people with information about genetic disorders, family planning, and risk of passing on a disorder.


Talk About Your Concerns

Don't be afraid to talk about NF in your family. You may also want to talk to your friends about your concerns. Be prepared for the possibility that your friends or family may not be as understanding or as supportive as you might hope. They may not be ready to talk or want to believe there is a problem. They may not know what to say. Some family members may feel guilty or angry about having a genetic disorder.

Unfortunately, there are some situations where you will need to be cautious about discussing NF.

Employers may discriminate against people with NF, even against parents of children with NF, because of potentially higher health insurance costs. Schools may be unsure how to treat a child with NF unless they are given specific instructions. Offer information about NF to people as it seems necessary. You also need to be careful not to overemphasize NF so that affected family members do not feel different from the rest of the family. Remember, the majority of the people with NF are not sick or handicapped, and can lead normal, functional lives.

It is important to accept that you or your child has NF and it may take time. Many other families have gone through similar problems. Local NF groups can be a source of tremendous support and advice. There are NF support groups in many states. These organizations were formed by parents and individuals with NF to provide support, advice, and information on dealing with many aspects of NF. They are important patient advocates.



You can find support through NF groups like the NF Network. There are many opportunities to get together and and learn from other NF families or to raise awareness and funds for the cause.



Teens with NF may benefit with others with NF

What to Do if You or Your Child Has NF1

People with NF1 will need regular physical exams to check vision, blood pressure, and spine to evaluate any new problems or changes. Sudden changes in the size of a neurofibroma, pain, weakness, or headaches should be brought to your doctor's immediate attention.

In young children, attention should be given to growth, hearing, vision, speech development, long bones, and spine. Parents should ask teachers if their child is having trouble with schoolwork, and whether a learning evaluation is needed. Early detection and treatment of learning problems is critical.

In older children and young adults, plexiform neurofibromas need to be checked and MRIs may be appropriate. Time needs to be set aside to talk about self-esteem and relationships with friends.

NF1 can cause difficulty with learning. The most common problems are short attention span, difficulty with visual perception, spelling, and arithmetic.

Young adults as well as teenagers should understand they can pass NF on to their children.

Scans of the brain, eyes, and spine can be helpful in NF1 if patients have symptoms that suggest problems in those areas.

Because NF1 causes spots as well as small tumors on the skin that are visible, people with NF1 may have to be braver than other people. Children with NF are sometimes isolated, rejected, or teased. If this occurs, the best thing to do is to talk about NF with your family, the child's friends and teachers.

If you are a parent of a child with NF, you should realize that your child may be frightened or angry about changes in his or her body. It is not helpful for you to pretend there is no problem. Simple, truthful, and positive explanations are reassuring to children such as "You have a problem that causes spots and some bumps on your skin. You need to see a doctor regularly to make sure everything is OK." You should talk in more detail with teenagers and make sure they are dealing emotionally with their disorder. They can tell their friends that the *café-au-lait spots* and bumps are not contagious.

What to Do if You or Your Child Has NF2

People with NF2 need regular physical examinations to check their hearing and neurologic function. Genetic testing is helpful in identifying milder cases, as well as genetic testing of tumor samples. Hearing tests and MRIs of the brain and spinal cord, and eye exams will probably be needed annually. Because NF2 can ultimately affect hearing in both ears, you will need to be open to several methods of communication. Sign language, lip reading and assistive technology offer many opportunities for the hearing impaired.

People with NF2 may need more than one complicated surgery. Because some surgery can lead to permanent disabilities such as loss of hearing, timing needs to be carefully considered. Surgery should be performed only by a neurosurgical or ear, nose, and throat team with special expertise in NF2.

The surgery itself can lead to complications in less experienced hands. Specially trained therapists, audiologists, ophthalmologists, and counselors are also essential in the rehabilitation process. In some instances, surgery should be delayed because tumors show very little growth over many years and can be watched carefully.

People with NF2 need to be cautious of non-standard treatments. Treatment of NF2 should always be discussed with physicians who treat many patients with NF2. While problems in NF2 can be frightening, there is evidence of significant improvements in treatment methods that are very encouraging and indicate real hope for patients to lead extremely functional lives. There is also a community of people who can provide advice and support.

Schwannomatosis is a rare condition that overlaps with NF2. Genetic testing can be helpful in patients with Schwannomatosis and may require testing tumor samples.



Guidelines for Children and Adults with NF1

Ages 1-5 years

1. Consult a doctor with knowledge of NF1.
2. Check long bones for bowing or fracture.
3. Watch developmental milestones and performance before preschool.
4. Have an eye exam annually.
5. Check blood pressure.
6. Assess other family members for evidence of NF.
7. Consider genetic testing for the NF1 gene.

Ages 6-14 years

1. Watch school performance.
2. Consider tests for learning disabilities or hyperactivity.
3. Check back for curvature.
4. Have an eye exam annually to age 10.
5. Have a hearing test.
6. Monitor height, weight, and sexual development.
7. Monitor changes in or appearance of neurofibroma.
8. Discuss self-esteem and relationships with friends and classmates.
9. Set aside time to talk about NF and how to respond to questions by friends.

Ages 15-20 years

1. Monitor changes in or appearance of neurofibroma.
2. Continue to talk about NF, relationships with friends, and self-esteem.
3. Discuss inheritance of NF and the likelihood of having a child with NF.

Adults

1. Watch for changes in tumors as these could be signs of cancer.
2. Watch for headaches, weakness, pain, or changes in sensation.
3. Check blood pressure.

Guidelines for People with NF2

1. Consult a doctor with knowledge of NF2.
2. Consider genetic testing for NF2.
3. Have MRI of brain and entire spinal cord annually.
4. Have annual hearing tests.
5. Have careful neurologic exam annually.
6. Have eye exam for cataracts and retinal abnormalities.
7. Learn signing or alternative forms of communication.
8. Evaluate other family members for vestibular tumors.
9. Discuss inheritance of NF2.
10. Discuss potential impact of NF2 on career and family.
11. Assess resources and support needed for daily living.

Provided by
Neurofibromatosis Midwest
www.nfmidwest.org
630.945.3562

**To find more information, an NF doctor
or a local NF Network affiliate,
visit us at www.nfnetwork.org
or call 630-510-1115.**