



## **Introduction**

**Neurofibromatosis** (NF) is a collective name for a group of genetic conditions in which benign (non-cancerous) growths or tumours affect the nervous system. Neurofibromatosis occurs all over the world and affects men and women equally.

There are two types of Neurofibromatosis: NF1 and NF2. They are two completely different conditions and people who have NF will have one type or the other. **This booklet is about NF1 only.**

**Neurofibromatosis type 1 (NF1)** is a very common genetic condition. Approximately 1 in every 2,500 people is born with NF1.

**NF1 varies widely in how it affects those who have the condition. Many people with the disorder will be affected very mildly** and may have nothing more than skin changes. A minority of people (around a third) who have NF1 will have medical problems related to the disorder at some time in their life. Some of these problems will be mild and easily treatable and others will be more severe.

## **How is NF1 diagnosed?**

The way the doctor can tell if a person is affected with NF1 is to examine him or her to see if there are signs of the disorder. There are specific features that the doctor will look for. NF1 usually appears in childhood and the diagnosis is confirmed if two or more of the following signs are present:

- Six or more flat, café au lait patches (brown coffee-coloured skin marks), which are the size of a pencil top or bigger. These usually appear during the first year of life and can increase in size and number. Café au lait patches are generally harmless and there is no connection between the number or size of café au lait patches and the severity of the condition. They sometimes fade later in life.
- Neurofibromas (small benign pea-sized growths or lumps) on or under the skin. These are a common feature of NF1. They usually appear during adolescence and tend to increase in number throughout life.
- Freckles under the arm or in the groin. Again, these are harmless but can be another sign of NF1.
- Plexiform neurofibromas. These represent growths around large nerves and can first appear as a swelling.
- Lisch nodules – these are small pigmented areas in the iris (coloured part) of the eye. They are often not visible except during examination with an eye microscope called a slit lamp. Lisch nodules are harmless and never cause symptoms, but can help in making a diagnosis of NF1.
- Another close family member has NF1.

### **Why does a person develop NF1?**

In around half the people who have NF1, the condition starts up in the individual because a change has happened on one of their genes. This happens before birth and there is no known reason why it occurs. For these individuals, no signs of the condition are found in either of their parents, making it most likely that the gene change (mutation) has occurred for the first time in the affected person. This is known as a 'new mutation'. The other group of people who have NF1 have inherited the condition from a parent who has NF1.

In either case, at the moment, genetic blood tests are not routinely offered to check if a person has NF1. An experienced doctor diagnoses NF1 by physical examination. Sometimes the features of NF1 take time to appear and therefore it may not be possible to make an immediate diagnosis of NF1. You or your child may be asked to come back to see the doctor on another occasion to be certain of the diagnosis. This can be a frustrating and anxious time for parents or adults who are under investigation; however, your doctor will want to be sure that the diagnosis of NF1 is correct.

NF1 does not skip generations. There are two ways in which it occurs: it crops up out of the blue as a first event in an individual or it is inherited from an affected parent.

### **How does NF1 affect the body and what can be done about this?**

If someone has NF1, he or she will have it for life. There is as yet no specific medical treatment or gene therapy to cure, prevent or reverse the features of NF1.

Many people who have been diagnosed with NF1 never experience health problems. However, some people who have NF1 can develop some of the complications that are known to happen in this condition.

The development of some of these features is related to age and some complications can first appear in childhood. Specific complications can be treated medically or surgically depending on the problem. Research may lead to new treatments in the future.

**NF1 is a complex disorder and one of its features is how variable the condition is from one person to another, even within members of the same family. At present there is no way to predict how mildly or severely any individual will be affected; however, specific complications of NF1 respond best to early treatment.**

Although no medical test is available to predict the mildness or severity of NF1, please do not be influenced by television or newspapers, which depict NF1 as invariably severe. The media can sensationalise the condition, when the reality is that **an estimated two thirds of people with NF1 are mildly affected and live a normal healthy life.**

Overall, the vast majority of the complications faced by people with NF1 are not life threatening.

## **The specific complications that occur in NF1**

### **Ophthalmic (Eyes)**

NF1 can cause problems at the back of the eye in the form of an optic nerve tumour/swelling called an optic glioma, which is most likely to occur in early childhood, up to about the age of 7. An optic glioma is a non-cancerous growth that involves the cells of the optic nerve, the nerve that connects the eye to the brain. In optic glioma in NF1, there are often no symptoms. Sometimes there can be vision problems or occasionally it can cause early puberty in a very small percentage of cases. Where this complication is diagnosed during childhood, it rarely progresses in adulthood, but it needs careful monitoring by an ophthalmologist (specialist eye doctor).

### **Orthopaedic (bones)**

In NF1 there can sometimes be problems with bone development. Specifically, NF1 can affect the growth and development of long bones, particularly the tibia (front lower leg bone or shinbone) or the bones around the eye. These problems, if they are going to occur in NF1, are usually seen in infancy and will not develop out of the blue in later years. There can also be a curvature of the spine (scoliosis) in NF1 and this complication can occur up until the child is fully-grown. Some orthopaedic complications of NF1 require a referral to an orthopaedic surgeon.

### **Dermatological (skin)**

Neurofibromas are benign tumours / growths that develop on or under the skin or along a nerve. They can occur anywhere on the body where there are nerves. They may look and feel like small pea-sized lumps or nodules under the skin. Skin neurofibromas are usually soft and painless. Those that are under the skin are usually firmer to touch but are usually also painless. Other neurofibromas may be deep in the body and cannot be felt from the outside. They do not cause health problems generally although some may press on a nerve and symptoms may develop such as pain or numbness. In this case, you need to see your doctor.

Many adults feel embarrassed and self-conscious about their neurofibromas. These nodules usually develop over time and can continue to grow in size. Typically, adults with NF1 will acquire more neurofibromas as they age because they do not go away.

There is no way to predict how many neurofibromas a person with NF1 will develop or when or where on the body they will develop. This feature of NF1 varies greatly from person to person. There is nothing a person can do to prevent or slow the growth of neurofibromas. This is one of the features of NF1 that doctors are currently researching. Sometimes a neurofibroma can be annoying because it is in an awkward place and may catch on clothes and it may be possible to remove it surgically. This should always be done by a doctor who has experience of NF1. You need to approach your GP first to ask for a referral. Although many people with NF1 tend to tan easily without sunburn it is important to use a high factor sun block and sun protection, as prolonged exposure to the sun may increase neurofibromas in later life

### **Plexiform neurofibromas**

Some neurofibromas can grow in a wide, spreading fashion around large nerves and may feel like a bunch of knots or cords beneath the skin. These types of growths are called plexiforms. Sometimes they will be obvious in early life as an area of swelling but other times they can lie deeper in the body and are harder to detect. They can grow anywhere on the body and, more rarely, occasionally on the face.

When they are present near the surface they sometimes grow to a large size. If this is going to happen it usually does so within the first few years of life. These tumours can be painful if knocked and can be disfiguring depending on their size and shape. Less commonly, a plexiform can become cancerous (more on this follows).

## Tumours and cancer

Everyone, whether they have NF1 or not, has a risk of developing cancer during their lifetime. It is known that a small number of individuals with NF1 will develop malignant (cancerous) tumours. However, the lifetime risk of someone developing cancer related to NF1 is around 10%. Research in this area is continually being updated. What health changes should you look out for? You should seek medical advice if you experience any new, significant or unusual changes in body habits which do not go away, just as you would if you did not have NF1. This could include a new or persistent pain, or a change in physical activities.

Skin neurofibromas are unlikely ever to become malignant. The plexiform neurofibromas are more at risk of becoming malignant. The signs to be concerned about if you have a plexiform neurofibroma are: sudden growth where there was previously slow growth; change in texture and the development of unexplained pain, for example: where the plexiform neurofibroma was not bumped or knocked. If the pain appears for no apparent reason and does not go away, this should be checked out. In rare cases, a person with NF1 can develop a brain tumour called an astrocytoma. Adults who experience persistent new headaches or a change in their usual physical abilities or activities (weakness, numbness, tingling in arms or legs, or a change in personality or memory) should seek medical advice.

## Hypertension (high blood pressure)

Occasionally NF1 can cause high blood pressure. **It is recommended that everyone with NF1 should have his or her blood pressure checked once a year throughout life.** Sometimes high blood pressure may not be related to NF1 and it is a **common** and **treatable** condition in adults who do not have NF1.

## Self image

Most people with NF1 have some signs of the condition visible on their skin. Many individuals have more obvious signs of NF1 than others and they can find the outward signs of the condition an extremely distressing burden to live with. There is no easy way to deal with this medically. Café au lait patches may increase as a child gets older but may fade in adulthood. They can be covered with clothes or make-up.

Skin neurofibromas can cause more obvious cosmetic effects. They can be removed by a plastic surgeon but there will be some scarring. They may or may not grow back and it would be impossible to remove all neurofibromas in someone who has a lot of them. Laser treatment can be used but, again, it is difficult if someone has a lot of neurofibromas. You need to ask your doctor for a referral to a specialist plastic surgeon or dermatologist to discuss what is possible for you as an individual. Camouflage make-up can sometimes help. This is a hospital-based service offered by the Red Cross and you can be referred by your GP. Many people find it helpful to talk through these sorts of issues. It is important to know that you do not have to feel alone with these difficulties and that there is support available.

## Pain and itching in NF1

For most people neurofibromas do not cause any problems. However, some individuals can experience pain and/or itching. Some adults with NF1 complain of chronic pain and this should be investigated medically. Back pain is sometimes related to a neurofibroma involving the spine and it might not be possible to remove this neurofibroma surgically. For an adult in whom chronic pain has been fully investigated, a referral to the pain clinic may be useful (ask your GP about this).

Pain-relieving medication can sometimes help in the management of this type of pain. Headaches can be a problem for some people with NF1. Again, medication may help. Itching sometimes happens in NF1 and no one knows why this is so. Medication such as antihistamines or a simple emollient can sometimes help – ask your GP for guidance. For more details, refer to the information sheet on pain in NF1.

## Learning and behaviour problems

Although intelligence (IQ) studies have shown that the vast majority of people who have NF1 are within the normal intelligence range, somewhere between a third and two thirds of people who have the condition will experience some problems with learning. It is the most common complication of NF1. However, it is important for parents to note that the majority of children who have NF1 are educated in mainstream schools and do not require special education.

Children and adults who have NF1 and who have learning problems may find difficulty reading and writing, they may find it hard to concentrate, have memory difficulties or have poor co-ordination. Where someone with NF1 has learning problems, this is often evident from their earliest years at school and, as children, they often underachieve at school and may have difficulties establishing and maintaining peer friendships. They can appear socially immature, have difficulties with concentration and sometimes be clumsy and uncoordinated.

There can sometimes be behaviour difficulties at home and at school. These difficulties can be similar to the difficulties found in children who do not have NF1, where there are conditions such as dyslexia, dyspraxia (clumsiness) and attention difficulties. It is important that these problems are recognised as early as possible so that teachers are aware of how NF1 can affect school performance. It is useful to have a frank discussion with the teacher so that common misconceptions about NF1 can be dispelled and the child can get help in school if he or she needs it.

Learning and behaviour problems in NF1 are not progressive, that is: they do not get worse over time. In fact, they can usually be improved with appropriate help. (More information can be found in the booklet that deals specifically with learning difficulties.)

## Deciding to have children if you have NF1

NF1 is caused by a change in the structure of a gene. Each person has about 30,000 genes in their body. Genes are the set of instructions within cells that tell the body how to grow, develop and function. Most genes come in pairs, so we all have two copies of the NF1 gene. If a person has NF1, one of these copies will have an alteration or spelling mistake and when someone with NF1 has a child, he or she passes on one of his or her two copies of the gene: either the normal one or the copy with the NF1 alteration. If the normal copy of the gene is passed on, the child is very unlikely to have NF1. If the altered NF1 gene is passed on, the child will have NF1. **Therefore, every person with NF1 has a 50:50 or 1 in 2 chance of passing the condition on to any of his or her children, boys or girls (similar to tossing a coin).**

For adults with NF1 who are planning their family, there is no way of telling beforehand how mildly or severely a child who inherits NF1 will be affected. The decision whether or not to have children is a very personal one for a couple and may depend on personal experience of NF1.

It is not usually possible to offer tests in pregnancy but couples considering this need to be referred to a genetic centre to discuss this with a genetic doctor and counsellor before contemplating a pregnancy. The doctor and/or counsellor will discuss the condition, the risks and the options available, so that the couple has all the information they need to make a decision.

## NF1 and pregnancy

There are no specific concerns about pregnancy and NF1. If you are pregnant and you have NF1, you should let the maternity unit know that you have NF1 at the first antenatal visit. Some women report an increase in the number of neurofibromas and an increase in size of existing neurofibromas. When your baby arrives, he or she should be checked for features of NF1 from the first months of life by a community or hospital paediatrician, geneticist or clinic specialising in NF1.

## What do I need to do to look after myself or my family if we have NF1?

If you have NF1, you should expect to live a long life in good health. Most people who have NF1 go through life with relatively few medical problems. NF1 can cause life-threatening problems but these are very rare. It is important to have regular medical follow-up so that any complications can be identified early. The problems in NF1 can be stable for many years but will not disappear and can sometimes increase.

## Professionals important to your care if you or your child has NF1 are:

### Family doctor (GP)

It is important to note that your GP may not see many people with NF1 and for this reason he or she may not see how variable NF1 can be from person to person. Medical guidelines can be sent to your GP to give him or her more information. **If you are an adult, it is a good idea to see your GP once a year for a general health check up and to have your blood pressure checked. It is also a good idea to have regular eye check ups with your optician.** See your doctor if you have any new or unexplained symptoms, just as you would if you did not have NF1.

### Hospital or community paediatrician (children's doctor)

**If you have a child with NF1, it is advisable that his/her growth, development and general health are monitored by a Community or Hospital Paediatrician from diagnosis until he/she reaches adulthood.** The paediatrician will advise you how frequently your child needs to be reviewed.

Brain scans are not routinely performed in NF1 unless there are specific reasons. If you notice any changes in your health (as described earlier) outside of routine review appointments, it is advisable to seek medical advice. If symptoms do not go away, then it is important to return to your doctor for further advice because if you do not, he or she will assume that you have recovered from the problem that you first went to see him or her about. It is worth reminding your doctor that you have NF1 and asking if your current health problem or symptom could possibly be related to the condition and if you need referral to a specialist.

### NF Specialist Advisor

The NfA funds jointly with the NHS a number of NF Specialist Advisor posts. **The NF Specialist Advisor service offers support and information which is available to families and individuals who have NF1.** The NF Specialist Advisor can speak with you by phone or can visit you at home. The service also has links with many other health and education professionals. The Specialist Advisor can visit your child's school to give information to teachers on learning and Nf1 or contact other health professionals who are working with you to give them information about NF1. The service is offered to all families in the UK and you are welcome to make contact by phone in the first instance. You will find contact numbers at the bottom of this page.

## Conclusion

We hope you have found this booklet useful. **It is important to remember that this is an introduction to NF1 and not all of the information will apply to everyone who has NF1.** For specific information, it is advisable to seek advice from the doctor who is treating you or your child. You can also speak to the NF Specialist Advisor for advice.

**This booklet has been written as a general guide to NF1 and tries to address some of the questions and concerns that people have when an adult or child has been diagnosed with NF1.**

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