Neuro fibroma tosis
ASSOCIATION OF IRELAND

The Child with NF1

NEUROFIBROMATOSIS: Tell-Tale Signs

Café-au-lait patches, 6 or more consult your Doctor

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Contents

Professor Green
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"I am delighted to support and endorse the new information sheets for people with Neurofibromatosis 1 and their families. The information will be of great help to the many families in Ireland with NF1, and will help those families to understand better the many ways in which Neurofibromatosis 1 can affect people. The National Centre for Medical Genetics is delighted to be associated with the Neurofibromatosis Association of Ireland, and that the Neurofibromatosis Association of Ireland has funded a genetic counsellor to run a specialised NF clinic in the NCMG. The NCMG has a wealth of experience with Neurofibromatosis and sees many families with the condition throughout Ireland. The NCMG holds genetics clinics in Dublin, Cork, Limerick and Galway, and is happy to see families with NF1, with a referral from their own doctor.

Prof. Andrew Green

NEUROFIBROMATOSIS CLINIC

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INTRODUCTION

Learning that a child has, or may have, Neurofibromatosis type 1 (NF1) can be very difficult. Often the diagnosis comes as totally unexpected news about a child who is healthy. The child may have some pigmented spots on the skin, which perhaps have been overlooked for years and assumed to be nothing more than simple birthmarks. Suddenly, the diagnosis of NF1 makes everything seem uncertain. Many parents find that time and knowledge help the healing process that follows the natural sense of grieving that comes with news of any medical condition.

It is helpful to note that the majority of children born with NF1 lead long and healthy lives, with relatively mild symptoms. Others will have more serious complications, but many of these are correctable – especially with early detection and intervention. NF1 research is progressing rapidly, bringing hope that effective new treatments will be found for this common, yet traditionally under-recognised disorder.

As a parent, whether you have NF1 yourself or have never even heard the word Neurofibromatosis until now, an unfortunate yet common reaction is to feel a sense of guilt. Parents often wonder if there is something they did to cause NF1, such as exposure to X-rays, medications, alcohol, or other factors. For this reason, it is helpful to recognise that NF1 always occurs as the result of a genetic mutation for which no known environmental cause has been found. The purpose of this brochure is to help make the uncertainties of NF1 easier to live with and understand, to take some of the mystery out of the disorder, and to help put the diagnosis in perspective.

What follows is a framework to help parents learn how NF1 may affect children as they grow and develop, what to look for, and how the disorder can be managed.

ACKNOWLEDGEMENT

The Neurofibromatosis Association of Ireland wish to acknowledge the assistance received in the preparation of this booklet from Professor Andrew Green, Director, Centre of Medical Genetics, our Genetic Counsellor, also the Children's Tumour Foundation, New York, and the many research scientists involved in the publication – names listed separately.

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THE CHILD WITH NF1

DIAGNOSIS OF NF1

The most common way that a child is diagnosed with NF1 is by the presence of multiple café-au-lait patches on the skin. Sometimes these are noticed at birth, but more typically they begin to appear in the first few months of life through a period of several years. The spots in themselves are harmless. Children with NF1 usually have many café-au-lait patches, and almost always six or more. There is no connection between the number of café-au-lait patches and the degree of severity of NF1. Although the presence of multiple café-au-lait patches strongly suggests the diagnosis of NF1, it does not prove it. There may be rare individuals who have as many as six café-au-lait patches but who do not have other features of NF1. The diagnosis of NF1 can only be made if another diagnostic feature of the condition is present as well. For example, a child with six café-au-lait spots who also has Lisch nodules in the iris of the eye would be considered to have NF1.

One problem with using standard clinical diagnostic criteria is that many features of NF1 are age-related.

They are often not present in very young children, but only appear with time. However, we would expect to see clear signs of NF1 by five years of age. Genetic testing for NF1 is possible but is not done routinely as part of the diagnostic process. The vast majority of people with NF1 can be diagnosed by a clinical examination of the skin and sometimes an eye exam can help us to confirm a diagnosis. Genetic testing can be useful is a small number of cases where a diagnosis of NF1 is suspected but the presentation is not typical.

PROGNOSIS OF NF1

NF1 is truly an unpredictable disorder. It varies widely in severity from one person to the next, and even between two people in the same family. Some go through life with only spots and a few bumps on the skin, and may be completely unaware that they have NF1. Others may have major medical complications or cosmetic problems due to the disorder, and these may begin at any time in life – at birth, or not until adulthood. Such uncertainty makes it very difficult to know what to expect for a young child who only has café-au-lait patches.

It is important to keep in mind that severe complications of NF1 are rare. The majority of children with NF1 have relatively mild manifestations. Many will experience some degree of cosmetic impact from the condition, but in most cases this is manageable without being overwhelming. Some complications of NF1 are apparent early in life and can be ruled out if the child does not develop them by a certain age, as discussed later in this brochure.

MANAGEMENT OF NF1

There is, at present, no cure for NF1. However, research is advancing rapidly toward the goal of developing new treatments, including safe and effective drug therapies. Until this is achieved, medical management of NF1 focuses on the early

detection of complications which can be treated – such as surgery to remove or reduce the size of neurofibromas, or assessment and intervention for learning difficulties.

A child with NF1 should have a complete medical evaluation at least once a year by a paediatrician who is familiar with NF1 and has access to appropriate specialists to help deal with problems, if found. The child's learning and cognitive development should be monitored and discussed from an early age. Due to a higher incidence of hypertension in those with NF1, blood pressure should be checked periodically from early childhood through adulthood.

All of this applies not only to the child with confirmed NF1, but also to a child in whom the diagnosis is suspected but not confirmed. Such a child may well be at risk of developing complications and should be followed just as though NF1 has been confirmed.

Often the question is raised, "Should all children with NF1 have X-rays, CT scans, or MRI scans?" There is no single "correct answer" to this question. It is generally agreed that any signs of neurological problems should be fully investigated, and often this includes obtaining a CT or MRI scan of the brain. Most physicians feel that scanning is unnecessary in the absence of specific signs of problems, since in such situations it is unlikely that treatment would be initiated.

COMPLICATIONS OF NF1

Some of the more common complications of NF1 are described below, according to the age at which they are most likely to appear.

Newborns and Infants

Most newborns with NF1 show few or no signs of the disorder. Café-au-lait patches may be noticed in the first few weeks of life. However, their absence in a newborn at risk for inheriting NF1 from a parent is

not a good indication that the baby is free of NF1, since the spots may appear later.

Neurofibromas, a common form of benign growth seen in NF1, are not often found in infancy. One exception is the plexiform neurofibroma which may appear as a soft swelling under the skin. There is some evidence that most plexiform neurofibromas are present from birth, but not all will be noticeable particularly if located deep inside the body. Any new signs or symptoms should be investigated. Particular attention should be paid to any sudden growth of, or pain in, a plexiform neurofibroma.

In rare cases, NF1 is associated with certain types of bone deformities, which typically arise at birth if they occur at all. These include deformity of the facial or leg bones. Infants may have a bowing or curvature of the lower leg (called tibial dysplasia). Some degree of curvature is normal, but an excessive degree or unusual direction of bowing indicates the possibility of this problem. If dysplasia is suspected, an X-ray is usually taken. If the condition is found, the child should be referred to an orthopaedic surgeon. The abnormal region of the tibia is very prone to fracture and may not heal well, requiring the attention of a specialist.

Another rare deformity typically evident from infancy is abnormality of the bony wall behind the eye, called the orbit. This condition, known as orbital dysplasia, can cause cosmetic problems that are to some extent correctable by plastic surgery. Some newborns with NF1 have a defect of the bone behind the orbit, called the sphenoid, as confirmed by X-ray or CT scan. This may be associated with bulging, recessing, or downward displacement of the eye. In addition, there may be a plexiform neurofibroma within the orbit and enlargement of the upper eyelid. This can be deforming, and often tends to grow over the years. If these bone problems

are not obvious in childhood they do not develop in later years.

NF1 can also affect the cardiovascular system and congenital heart defects can be seen in some children. Most often the valves of the heart are affected, particularly the pulmonary valve. Problems with the heart can frequently be detected at an early age when a heart murmur is heard during a routine examination. When a heart defect is suspected, a paediatric cardiologist should be consulted and a full evaluation should be done.

Preschool Years

Café-au-lait patches usually are visible by this age, if not in regular light then with the aid of a Wood's ultraviolet lamp used by dermatologists and geneticists. Plexiform neurofibromas may grow, or may be noticed for the first time. Sometimes a few freckles may be seen in the armpits or groin, a further indication of NF1, and a few small neurofibromas may be noticed on the skin which are soft to the touch and have a pink or purple hue. They are not painful and rarely cause problems other than cosmetic ones. Some children develop multiple neurofibromas early in life, but they do not necessarily experience additional or severe complications of NF1.

Children with NF1 can sometimes be shorter than would be expected from the height of others in their family. The cause of this short stature is not known; medical testing is rarely productive, except in cases where growth rate suddenly and unexpectedly changes. Children with NF1 can sometimes have increased head size. This generally does not cause discomfort to the child, and is usually not correlated with neurological problems. The head grows at a faster rate than normal, but at a steady, consistent pace. As long as this is the case, it is usually not necessary to perform an examination such as a

CT scan. In rare instances, the head growth may be associated with vomiting or headache. In such cases, a CT or MRI scan is usually done to be sure that increased pressure of fluid inside the brain (a condition called hydrocephalus) has not developed.

Brain tumours in NF1 can occur at any point in life, including early childhood. Fortunately, they are not common. Optic gliomas are tumours that form on the nerves of the eye. They are the most common brain tumour in children with NF1. They typically appear in the first decade of life but can develop later. Most do not cause symptoms and require no treatment; but if a problem does arise it may cause loss of vision, pain, bulging of the eye, or abnormal pituitary hormone secretion. Abnormal hormone secretion can lead to early or late puberty and should be evaluated by a medical expert. Symptomatic optic gliomas are diagnosed by CT or MRI scanning and can be treated, usually by chemotherapy. It is not uncommon to find thickening of the optic nerve in children with NF1 who have no signs of optic glioma. Only rarely do symptoms of progression occur, requiring treatment. It is recommended that all children with NF1 have ophthalmologic (eye) exams performed annually.

Developmental delay, and speech or motor problems, should be addressed as soon as they are suspected. Early intervention by speech therapists, occupational therapists, physiotherapists and educational psychologists can be very effective. Parents suspecting such problems should seek a thorough neuropsychological evaluation of their child to ensure early diagnosis. Intellectual impairment is a rare complication of NF1 which is generally apparent by the preschool years.

School Age
Any of the features of NF1 mentioned above may begin or continue to appear throughout the school

years. It is not unusual to become aware of learning difficulties in the school-aged child, as this is one of the most common of serious problems related to NF1. Roughly half of all children with NF1 have some form of learning difficulty (LD). By definition, LD involves learning problems in children of average or above average intelligence. The management of LD in children with NF1 is the same as for any child with a learning problem. Behavioural problems, including hyperactivity and attention deficit, are also common in NF1. Children with NF1 may need extra help building social skills, as they may not be able to discern subtle, non-verbal social cues as well as others.

While learning difficulties may not surface until the child is in school, and may become more apparent as academic expectations grow, they are not progressive. That is, they do not worsen over time. In fact, with early and appropriate intervention, skills typically improve and progress is made in school. Additional brochures about education issues and learning difficulties associated with NF1 are available for parents and educators from NFA Ireland.

Lisch nodules may also develop in older school age children or in adolescents. These are small raised areas on the iris or coloured part of the eye. Often they can only be detected by an ophthalmologist with a specialized slit lamp examination. Lisch nodules are found in almost all individuals with NF1 by adulthood. They are benign and do not cause any problems with vision.

Rarely, NF1 can affect the blood vessels. The renal artery which takes blood to the kidney is most frequently involved. High blood pressure (hypertension) can develop if there is narrowing of the renal artery, so blood pressure should be monitored by the paediatrician on a regular basis throughout childhood. A variety of methods are available for treatment of high blood pressure in

these cases. Scoliosis, or curvature of the spine, is more common in children with NF1 than those in the general population and may appear at an earlier age. It is wise to screen children with NF1 for scoliosis throughout childhood, as there are ways to effectively treat this condition.

Adolescence
Adolescence is generally a time of change, and often this includes a change in the manifestations of NF1. Individuals who have not developed neurofibromas during childhood often begin to see them appear on the skin during puberty. Pre-existing plexiform neurofibromas often grow at this time. Skin freckling may also increase. The cause of these changes is not well understood, but it is believed that changes in hormones may be responsible.

The teen years can be a challenging time for anyone, but the multiple burdens of NF1 can lead some adolescents to feelings of depression, anxiety and social isolation. Counselling and assisting the child in finding a social network can help significantly. The American Children's Tumor Foundation offers a YouthCONNECT program which includes an online youth chatroom. A printed brochure for teens is also available to help children with NF1 better understand and manage the disorder.

RARE LIFE-THREATENING COMPLICATIONS

As previously mentioned most individuals with NF1 live long and generally healthy lives. Yet it must be recognised that some rare complications of the disorder can be considerably more serious, even life-threatening. Neurofibromas are not cancerous tumours; they do not spread through the body. In some children, however, cancer may develop within a plexiform neurofibroma.

Signs of malignancy include sudden growth of a mass, or the onset of pain in a previously painless mass. It is common for plexiform neurofibromas to be painful if bumped or otherwise traumatised; but this is different from the pain associated with malignancy, which is more likely to occur spontaneously without evidence of injury to the mass. Likewise, not all growth indicates malignancy. Benign neurofibromas commonly grow in size, especially plexiform neurofibromas. Sudden growth of a portion of the neurofibroma is more indicative of malignancy than slow, steady growth of a larger mass.

Malignancy related to NF1 is estimated to occur in about 8-13% of affected individuals throughout the course of their lives. Although this might seem like a large number, it must be compared with the fact that 40% of all people – with or without NF – will develop a malignancy sometime in their lives. Cancer related to NF1 usually can be treated with a combination of surgery, radiation, and chemotherapy. The outcome depends largely on how early the malignancy is detected.

Tumours in the brain and spinal cord occur in relatively few persons with NF1, although the risk is higher for children with NF1 than for those in the general population. Brain tumours are usually detected after symptoms such as headache, vomiting, seizures, visual disturbance, or behavioural changes are present. It should be emphasised that not all headaches in children with NF1 mean that a brain tumour is present. Ordinary headaches, tension headaches, and migraines occur at least as commonly, if not more often, in persons with NF1 as in the general population. Persistent or especially severe headaches should be reported to a physician. A tumour can be diagnosed by CT or MRI scan.

Another uncommon, yet potentially serious complication of NF1 is having an abnormal blood

vessel in the brain, a condition known as cerebral vasculopathy. Anyone with NF1 who suddenly develops a neurological deficit, whether motor or sensory, should be evaluated promptly – for this may indicate a blood clot or obstruction.

TELLING A CHILD ABOUT NF1

One of the most common and difficult questions asked by parents of children with NF1 is when and how to explain the disorder to the child. There is no single correct approach to this. Much depends on the adjustment of the parents, the maturity of the child, and the specific manifestations of NF1 present in the child. If any general advice can be given, it is to answer the child's questions honestly, giving as much information as the child asks for or seems able to understand.

One need not go into great detail about possible complications of NF1 with a young child; but evasive answers often provoke fear rather than provide reassurance, and false answers may impair later trust. Sooner or later the child will learn about NF1, if not from his or her parents, then from friends or the media. This can lead to misinformation and consequent fear well out of proportion with the risks associated with the disorder. If parents and physicians serve as the main source of facts about NF1, one can be more certain that the information is accurate and balanced.

TELLING TEACHERS ABOUT NF1

Parents sometimes worry about telling the school that their child has – or may have – NF1.
They fear that their child may be inappropriately "labelled". Actually, it is more common for harm to be done by not informing teachers – and having

them fail to recognise learning difficulties or mislabel a child as a "behaviour problem" that parents should better control. A frank discussion with a child's teachers can often correct common misconceptions about NF1, and lead to earlier detection and treatment of learning problems related to the disorder.

GENETIC IMPLICATIONS OF NF1

Roughly half of all cases of NF1 are inherited from a parent who has the disorder. The other half result from a random genetic change (spontaneous mutation) most often in the egg or sperm cell that created the child. Regardless of how NF1 occurred, all individuals with the disorder have a 50% chance of passing on NF1 to each of his or her children. Naturally, these 50-50 odds remain true for each subsequent pregnancy.

Even if a child appears to be the first in a family to have NF1, it is important to determine if one of the parents may, in fact, also have the disorder – perhaps a case so mild it has gone undetected. The best way to resolve this question is for a doctor to examine both parents, typically through a skin examination looking for café-au-lait patches and an eye examination looking for Lisch nodules with a slit lamp.

If neither parent is found to have signs of NF1, the child's case most likely results from a new mutation. In this instance, it is highly unlikely that the parents will have other children with NF1, although it is not impossible for this to happen. Brothers and sisters of any child with NF should be examined for signs of the disorder, to be sure.

Genetic testing for NF1 is not part of the routine diagnostic process but can be useful in a small number of cases if the diagnosis of NF1 is uncertain.

Some families wish to consider prenatal testing in a pregnancy or an In-Vitro Fertilisation (IVF) technique called Pre-implantation Genetic Diagnosis (PGD). Before these procedures can proceed genetic testing is needed in order to find the exact gene alteration which has caused the condition in the parent.

If it is decided that a child has NF1 on the basis of new mutation of the gene, it is natural to ask, "How did this happen?" The cause of mutations in the NF1 gene is unknown. Again, no environmental exposure has yet been implicated as a cause. In fact, genetic mutations occur commonly as a natural biological process. Whenever a cell divides, an enormous volume of genetic information must be copied properly. It is not unusual for a bit of information to be copied incorrectly, resulting in a mutation.

SOURCES OF SUPPORT

Understanding medical facts about NF1 may be the first step towards adjustment to living with the disorder. It is therefore important to maintain open communication with health professionals who are involved in caring for a child with NF. Family and friends can likewise be sources of support. NFA Ireland can provide information as well as opportunities to meet others who are dealing with the condition and can share their experiences, concerns and advice.

HOPE THROUGH RESEARCH

Research on NF1 has progressed rapidly and has entered an exciting phase. This is due largely to the application of new techniques of genetics, which led to identification of the gene for NF1 and to advances in understanding cell biology relevant to the disorder. Such discoveries have already resulted in new methods of diagnosis.

The likelihood of finding effective treatments for NF1, in the years ahead, is promising. Scientists are actively researching the disorder at centres throughout the world.

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NF1 BROCHURES
- OVERVIEW OF NEUROFIBROMATOSIS TYPE 1
- A GUIDE FOR EDUCATORS
- LEARNING & COGNITIVE DIFFICULTIES
- NEUROFIBROMATOSIS TYPE 1 FOR TEENS
- THE CHILD WITH NEUROFIBROMATOSIS TYPE 1
- TALKING TO YOUR CHILD
- READERS 100 QUESTIONS ANSWERED

LEAFLETS
- NF1 REVIEW CHECKLIST FOR CHILDREN & ADULTS
- NEUROFIBROMATOSIS – A BRIEF INTRODUCTION
- SCHWANNOMATOSIS
- CONTACT FORM

CLINICAL GUIDELINES FOR MANAGING NF1
- FOR ADULTS
- FOR HEALTH PROFESSIONALS

NEUROFIBROMATOSIS TYPE 2 BROCHURES
- FOR FAMILIES
- FOR HEALTH PROFESSIONALS

HANDBOOK
- NF IRELAND HANDBOOK

Neurofibromatosis is a Little Known Genetic Condition and Can Manifest Itself in a Whole Lot of Different Ways

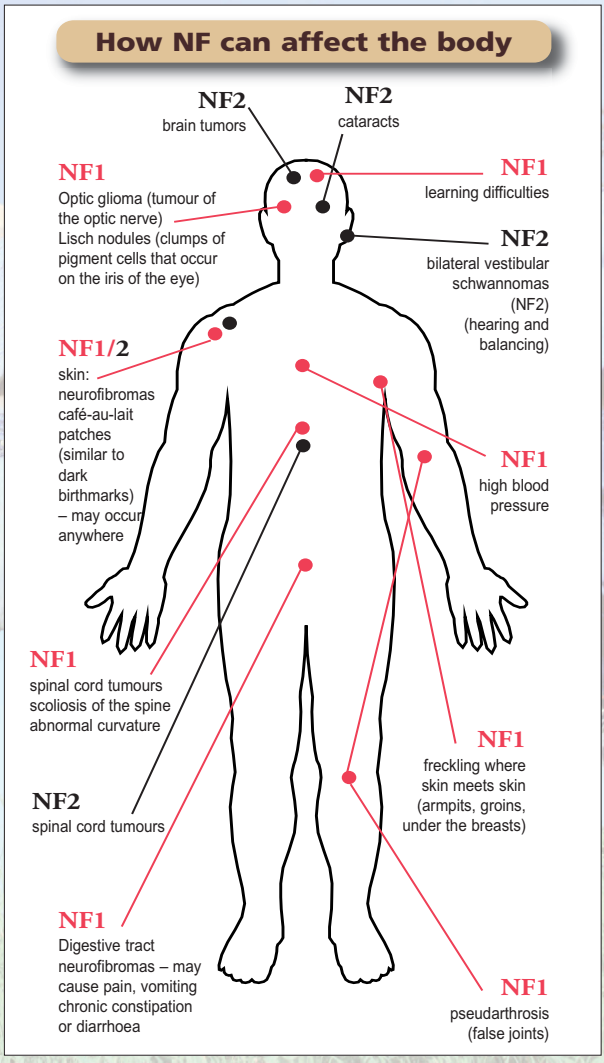
The care of persons with NF is made complex by the wide range of expression of the disorder. It is difficult to predict the specific problems that will occur in a particular individual. Diagnosis is made if an individual has two or more of the following features.

The diagnosis is based on the following clinical criteria:

1. **Six or more (café au lait)** coffee coloured patches sized 5mm or over in pubertal individuals and over 15mm in size in post pubertal individuals.
2. **Freckling** under the **arm** or in the **groin** area.
3. **Two or more Neurofibromas** of any type (growth of tumours on nerve tissue anywhere on the body) usually first seen on the skin.
4. **Plexiform Neurofibromas –** large bundle of nerves are thickened and appear as a soft tissue mass under the skin, these growths often large, can change the normal shape of the body.
5. **Optic Glioma –** Thickening of the optic nerve.
6. **Lisch Nodules –** clumps of pigment cells that occur on the iris of the eye.
7. **Orthopaedic** problems include **scoliosis** (curvature of the spine) **abnormal bone development**, such as overgrowth in long bones causing bowing and deformity that result in fractures, which fail to heal.
8. **First-degree relative with NF** e.g. parent, sibling, offspring.
9. **Learning Difficulties**. As many as 50% of children with NF have short attention span, appear clumsy and uncoordinated. Problems particularly with arithmetic and spelling are common.

Neurofibromatosis Type 2

Another rarer type of Neurofibromatosis and distinct in its clinical feature is **NF2.** The gene for **NF2** is located on chromosome 22, Features include: **Vestibular schwannomas** (tumour on hearing nerve). **Schwannoma** (type of tumour of the substance that covers nerve fibres). **Meningomas** (tumour of the covering of the brain). **Cataract.**



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