

Fact Sheet:

# Neurofibromatosis Type 1



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Neurofibromatosis Type 1 (NF1) is the most common single gene disorder to affect the human nervous system with an incidence of approximately 1 in 3,000 to 4,000 births. NF1 causes developmental changes in the nervous system, skin, bones, and other tissues. Half of the cases of NF1 result from a spontaneous genetic alteration, while the remainder of cases is inherited from one or both of the parents. NF1 occurs with equal frequency in males and females and has been identified in all ethnic, social and economic groups around the world.

NF1 affects each person differently. Some people are quite mildly affected and may not experience any impacting symptoms of the disorder while others are more severely affected and require increased medical treatment. Each individual with NF1 - even those in the same family - can be affected in a completely different manner. Overall, it is estimated that about half of the people with NF1 are moderately to severely affected. While it is very unlikely that any one person diagnosed with NF1 will experience all of the associated complications, it is difficult to predict the severity or progression of the disorder in any individual case.

NF1 is associated with a wide variety of complications affecting almost every system of the body, including the nervous system, the eyes, hearing, the skeleton, the endocrine system, the circulatory system and skin.

### **NF1 may present with manifestations such as:**

- Multiple café-au-lait spots
- Auxiliary freckling (freckling under arm)
- Lische nodules (freckles on the iris of the eye)
- Macrocephaly (large head circumference)
- Disfigurement due to dermal neurofibromas (skin tumours)
- Internal tumour growth
- Plexiform tumour growth
- Bone deformities
- Headaches, seizures
- Vision and hearing loss
- High blood pressure
- Pain/physical disability
- Learning disabilities
- Development delay
- Speech difficulties
- Psychosocial issues
- Impact on family
  
- Adjustment to living with chronic health issues and uncertainty

## Diagnostic Criteria for NF1

The signs of NF1 usually begin to appear in childhood or adolescence. The diagnosis of NF1 is based on the presence of two or more of the following:

- Family history of NF1
- 6 or more café-au-lait spots (flat, brown pigmented spots on the skin)
- Freckling under the arms or in the groin area (areas not exposed to sunlight)
- Lisch nodules (freckles on the iris of the eye)
- Presence of pea-sized bumps on the skin (cutaneous neurofibromas)
- Plexiform neurofibromas (tumour growth along the body's peripheral nerves)
- Skeletal abnormalities such as bowing of a leg or thinning of a long bone (bone dysplasia), or curvature of the spine (scoliosis)
- Tumour on the optic nerve (optic glioma)

Using the above criteria, the diagnosis can be made with certainty in 94% of patients by the age of six years old.

## Clinical Features of NF1

- **Café-au-lait spots** are the hallmark feature of NF1 and usually become obvious during the first two years of life. These skin lesions are flat coffee coloured patches on the skin. They develop anywhere on the surface of the skin and often become darker in sun exposed areas. They vary in size from that of a dime to very large. Generally, café-au-lait spots increase with age.
- **Skin fold freckling** is useful criteria, in combination with café au lait spots, for making the diagnosis of NF1 in young children. Freckling tends to appear during the first five years of life, in areas not exposed to sunlight. The reported frequency of axillary (armpit) freckling varies between 64% and 84%. Inguinal (groin) freckling occurs in 52% to 56% of NF1 individuals. More generalized freckling may also occur on the trunk and neck and in the sub mammary region of women.
- **Lisch nodules** are tiny lumps that form in the iris of the eye; they do not affect vision. They are often not visible, except with a special eye examination microscope (slit lamp). Lisch nodules are characteristic of NF1. They do not cause symptoms but are extremely useful as a diagnostic tool, particularly in adults. The incidence of Lisch nodules in NF1 increases markedly with age; by the age of five years, only 22% of patients have Lisch nodules, whereas by 20 years of age 96% to 100% of patients have Lische nodules upon a slit lamp examination.

- **Dermal neurofibromas (skin tumours) – cutaneous (on surface) and subcutaneous (under the skin)** are benign, usually small, lumps on or under the surface of the skin. These do not usually develop until preadolescence, with increasing tumour development during adolescent and the young adult years. Early neurofibromas may appear as “divots” in the skin, with reddening of the skin due to dilatation or an increase in the number of capillaries. In females there is often a clear history of an increase in number of neurofibromas during puberty and pregnancy, with an increase during puberty noted in males. In adulthood, the number of neurofibromas affecting an individual can range from just a few to thousands. While cutaneous neurofibromas may become a major cosmetic problem for individuals with NF1, they are not pre-malignant lesions and do not transform into malignant tumours. Plexiform neurofibromas on the other hand are usually congenital in origin and can undergo malignant transformation.
- **Short stature** is common to people with NF1 and not usually associated with growth hormone deficiency.
- **Macrocephaly** is a large head circumference common to people with NF1. Some instances of macrocephaly are accompanied by unexplained headaches for which the cause is not clear.
- **Specific learning disabilities** are present to some degree in approximately 60% of individuals with NF in a wide range of affect. Learning disability means that a child of normal intellect has specific problems in certain areas, for example, difficulty with reading or spelling or problems with fine motor co-ordination that can lead to incoordination and social skill issues. It is valuable for a child with NF1 who is having school difficulties, to have a neuro/psychological assessment to determine their strengths and weaknesses and determine what educational interventions may be of benefit.
- **Optic gliomas** are tumours that can affect one or both of the optic nerves, which carry visual information to the brain from each eye, and the optic chiasm, the area where the optic nerves cross each other in front of the hypothalamus of the brain. Optic gliomas are fairly rare and usually associated with NF1. Optic gliomas are slow-growing, non-cancerous and occur in children, almost always before age 20.
- **Plexiform tumours** are a less common type of NF tumour which grows along the body's peripheral nerves (the nerves that carry messages between the body and the brain). These tumours develop “roots” and can cause nerve involvement and disfigurement. Removal of these tumours can be very complex, as they intertwine with nerve fibers. Along with removing the tumour, the neurosurgeon is concerned about preserving nerve function. About 5 percent to 10 percent of the time, a plexiform tumour will degenerate into an MPNST – malignant peripheral nerve sheath tumour – a rare type of malignant soft tissue sarcoma. When a previously painless tumour becomes painful or grows rapidly, it may indicate the degeneration of a benign tumour into a MPNST.

- **Long bone dysplasia** is a fairly rare complication of NF1 that causes bending and thinning of one long bone of the body, usually the tibia. Other affected bones can be the fibula, radius, ulna, femur and clavicle. Should an affected bone break, natural healing is unlikely, causing a condition called pseudoarthrosis (meaning “false joint”). Fracture of these bones is difficult to treat. Braces and surgery are likely treatments in the prevention of pseudoarthrosis. Failure to heal, especially concerning tibial pseudoarthrosis, may require amputation in severe cases.
- **Scoliosis** is a curvature of the spine. In children with NF1, especially girls, scoliosis can develop into a rapidly progressive condition that may require surgery. Early detection of this condition can aid treatment with back braces in an effort to minimize the need for extensive surgery.
- **High blood pressure** is a concern for adults with NF1. The underlying cause of high blood pressure in NF patients can be different than the general population. Rarely, for NF patients, it can be caused by narrowing of the blood vessels entering the kidney (Renal Stenosis); decreased blood flow causes the blood pressure to rise. For these people, treating the symptoms of blood pressure rather than the narrowed vessels doesn't solve the problem. In a small percentage of NF patients, a growth on the adrenal gland causes very significant increase in blood pressure, and the growth needs to be removed.

## How is NF1 treated?

Treatments are presently aimed at controlling symptoms. The care and treatment of the physical aspects of NF often requires the expertise of various medical disciplines, including neurology, orthopedic, vascular and plastic surgery specialists among others. Removal of painful or disfiguring tumours is sometimes an option; however, there is a chance that the tumours may grow back and in greater numbers and nerve involvement must be considered. In the rare instances where tumours become malignant – 3 to 5 percent of all cases – treatment may include surgery, radiation or chemotherapy. Surgery can help some bone malformations and problematic scoliosis. Surgery may be combined with braces in these situations.

Resources are available for other issues presented by NF1 as well. Intervention for children who exhibit development delays and learning issues can be obtained, such as speech therapy, learning assistance and occupational therapy. Learning Disability Associations often offer appropriate workshops for both children and adults with learning disabilities and social skill issues.

The psychosocial impacts often accompanied by a diagnosis of NF, can also be alleviated with the responsible guidance and support of medical and educational systems and the utilization of peer support and community resources. Community resources are a vital link to possible assistance in meeting the needs of an individual. Keep open dialogue with your doctor, become educated about NF and reach out to your community. Help is available.