NF 1 – Neurofibromatosis 1

Research into improving treatments and finding cures for NF1 is ongoing but as neurofibromatosis cannot currently be cured, the goal is to monitor the condition and intervene when treatment is required.

Neurofibromatosis is a genetic condition that affects the skin, soft tissue, bone and nervous system. It is characterised by the development of soft tumours called neurofibromas that develop on the nerves and brain, or grow on, or under, the skin.

As they grow, the tumours can press on important areas in the body, affecting the way the body functions with varying degrees of severity. Neurofibromas are usually non-cancerous but in a small percentage of cases may become cancerous.

Neurofibromatosis is a genetic condition and can be passed from a parent to their child. However, about half of all cases are due to a new mutation in the gene that causes NF1.

NF1 is the most common type, representing about 90 percent of all neurofibromatosis cases. In New Zealand it is estimated that NF 1 affects about 1 in 3,000 people. It is caused by a defect in a gene on chromosome 17.

NF 1 may also be called von Recklinghausen disease – named for a German pathologist, Freidrich Daniel von Recklinghausen who, in 1882, first characterised the tumours in neurofibromas which consist of mingling of nerve cells and fibrous tissue.

NF1 is characterised by:

- Café-au-lait spots (light brown patches on the skin).
- Multiple neurofibromas.
- Freckling on the skin under the armpits and in skin folds eg: the groin.
- Tiny tumours in the iris of the eye (Lisch nodules).

NF 1 is usually diagnosed in infancy or early childhood.

Cutaneous neurofibromas are superficial, soft tumours that grow on the surface of the skin.

Signs and symptoms

The severity of the condition tends to vary greatly from person to person. Some people are barely affected by the condition, while others are severely disabled by it.

Approximately 60 percent of people with NF 1 will have only relatively mild signs and symptoms.

The most obvious signs of NF 1 are those that affect the skin – café-au-lait spots, freckling, and neurofibromas of the skin. Café-au-lait spots usually measure at least 5mm in diameter in children and can grow to 15mm in diameter in adults.

Neurofibromas are the hallmark of NF 1. There are four main types of neurofibromas, each classified by where they develop in the body.

Cutaneous neurofibromas are superficial, soft tumours that grow on the surface of the skin. Subcutaneous neurofibromas grow within the skin layers and can cause local tenderness. The other two types, called nodular plexiform and diffuse plexiform, develop within the body and can cause problems such as:

- Curvature of the spine (scoliosis).
- Malformation of the long bones below the knee and elbow.
- Vision loss.
- Bleeding or blockage in the gut.
- Seizures.
- Hydrocephalus (accumulation of fluid on the brain).
- High blood pressure.

Children with NF 1 have high rates of speech impairment, learning difficulties and attention deficit hyperactivity disorder. Puberty may be

early or delayed. Some cancers occur more commonly in people with NF 1. These include some malignant brain tumours, leukaemia, and cancers of the muscles, kidneys and adrenal glands.

Diagnosis

A diagnosis of neurofibromatosis is based on the characteristic signs of the condition and certain diagnostic criteria. A careful personal and medical history will be taken. For a diagnosis of NF 1 to be made, two or more of the following signs need to be present:

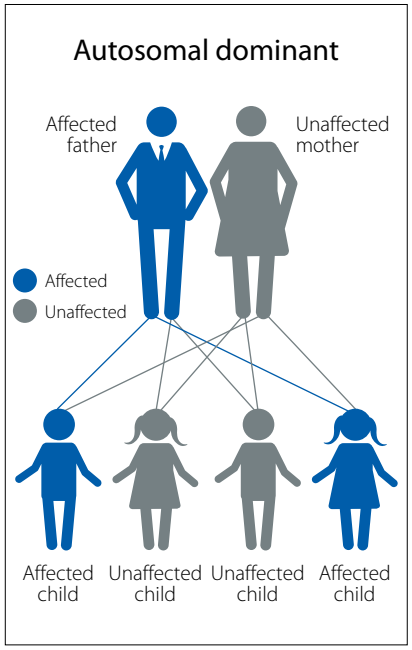
- Six or more café-au-lait spots larger than 5mm in diameter
- Two or more neurofibromas
- Freckling under the arm or around the groin
- Lisch nodules
- A tumour on the optic nerve
- Certain abnormalities of the skeleton
- A family member with NF 1.

Treatment

Research into improving treatments and finding cures for NF1 is ongoing but as neurofibromatosis cannot currently be cured, the goal is to monitor the condition and intervene when treatment is required.

As a general rule, tumours that do not cause any problems are usually left alone. If treatment is required, it usually involves surgical removal of tumours. Surgical removal may be performed if:

- Tumours cause discomfort and pain.
- Tumours keep getting irritated or damaged.



Mode of inheritance for for neurofibromatosis type 1.

- Tumours in the spine or brain are causing symptoms.
- Sensation or motor function is affected.
- A tumour is suspected, or known, to be cancerous.
- Skeletal abnormalities, such as scoliosis, may also require surgical treatment.

If tumours are disfiguring, plastic surgery can help to improve cosmetic looks.

Physiotherapy can be useful if mobility or function is affected. If there are deformities of the feet and/or legs orthopaedic devices can also help to improve mobility.

Some brain tumours or tumours along the nerves can be treated with chemotherapy or radiotherapy.

People with neurofibromatosis should have regular physical and neurological examinations. Attention should be given to monitoring changes in the size or number of neurofibromas.

Referral to Genetic Health Services is also useful.

Genetics of NF1

Approximately half of individuals with NF1 inherit the condition from one of their parents. The other half develop it as the result of a spontaneous (also called new or de novo) change in one of the NF genes in the egg cell or sperm cell during conception.

NF1 is inherited in an autosomal dominant way. This means that individuals with NF1 have a 50 percent chance of passing the condition on to their offspring. If a child inherits the NF gene, they will always show symptoms of the condition, however, it is difficult to predict the severity. This is called variable expressivity.

If a child of someone with NF does not inherit the NF gene, they do not have NF and therefore cannot pass it on to their future children. That is to say, NF cannot "skip a generation".

Research

There are several drugs that are being trialled looking to treat various aspects of NF1 and NF2. Visit clinicaltrials.gov and enter NF1 into the keyword search. ®