SEGMENTAL NF:
A Guide for Patients
Introduction

This brochure is written for those in whom a diagnosis of segmental neurofibromatosis (NF) has been made or is being considered. Segmental NF is a form of NF1 or NF2 in which the manifestations are limited to just a portion of the body. This brochure will answer common questions about segmental NF, including how the diagnosis is made, how patients should be followed and the risks that a person with segmental NF can have a child affected with NF.

What is Neurofibromatosis (NF)?

You may have heard of two different types of neurofibromatosis: neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2). The common features of each condition are listed below.

**NF1**

- Birthmarks (café-au-lait spots)
- Freckling in the armpits or groin
- Tumors that grow along the length of nerves, sometimes associated with overgrowth of part of the body (plexiform neurofibromas)
- Knots on the skin (dermal neurofibromas)
- Bony problems, including curvature of the spine (scoliosis), bowing of the leg (tibial dysplasia), or deformity of the bones around the eye (orbital dysplasia)
- Lisch nodules (tan bumps on the iris – colored portion – of the eye)
- Tumor of the optic nerve (optic glioma)

**NF2**

- Tumors on the 8th cranial nerves (vestibular schwannomas), causing ringing in the ears, hearing loss, or dizziness
- Tumors in the brain or spine (meningiomas, schwannomas, or ependymomas)
- Eye findings (cataracts)
What is Segmental NF?

Individuals with segmental NF will have only a certain area of the body that shows signs of NF. Any part of the body can show signs of segmental NF.

Segmental NF1 - Individuals with segmental NF1 most commonly have the skin findings associated with NF1, such as café-au-lait spots, skin fold freckles, or neurofibromas, confined to a certain area (for example, only an arm or only a restricted area of the back). Some patients may have an isolated tumor, such as a plexiform neurofibroma, without the other signs of NF1 throughout the body. It is not known whether such isolated tumors represent true cases of segmental NF, or whether they occur due to other unknown causes.

Segmental NF2 - Individuals with segmental NF2 will have some of the tumors associated with NF2 confined to a restricted region, such as only one side of the body.

How is a diagnosis of segmental NF made?

Both NF1 and NF2 are genetic conditions; NF1 is due to a mutation in the NF1 gene, whereas NF2 is due to a mutation in the NF2 gene. Individuals with NF1 or NF2 generally carry the mutation in all cells of their body, since the mutation was present from the time of conception in the fertilized embryo. In persons with segmental NF, in contrast, the mutation is present only in some cells of the body. This happens if the mutation was acquired during early development, leading to the body containing a mixture of cells, some with a mutation and some without. This is referred to as “mosaicism,” that is, the body is like a mosaic where there are two types of cells, one type containing a mutation and one type
not having the mutation. In persons with segmental NF, the region of the body in which cells carry a mutation will show features of NF, whereas other regions of the body (those with cells that do not have the mutation) will not show such features of NF.

**Neurofibromatosis**

During division of developing embryo, all cells have NF mutation, because it was present in original embryo.

**Segmental NF**

During division of developing embryo, a NF mutation is acquired*. Only the cells made from the mutant cell have the NF mutation, not all cells.
What are the complications of segmental NF?

Individuals with segmental NF can develop any of the complications of NF1 or NF2 in those regions of the body that include cells with the mutation. These can be very mild, or, in some cases, can include severe complications. Many individuals with segmental NF1 never develop any complications other than café-au-lait spots confined to a restricted region, but others can develop neurofibromas. Although it may appear that signs are limited to just one area, such as the skin on an arm or a leg, there is no way to be sure that there aren’t additional cells carrying a mutation deeper inside the body; therefore, additional complications of NF are possible, although less likely than in someone with NF in a non-mosaic form.

How is segmental NF managed?

At the present time, clinical management focuses on the specific problems that affect a particular patient. For example, surgery may be required in a child with a plexiform neurofibroma. An adult with dermal neurofibromas can see a plastic surgeon or dermatologist to have tumors removed. An optic glioma or schwannoma may need to be treated.
by an oncologist or neurosurgeon. Because of the wide variety of body parts that can be affected in a patient with segmental NF, most patients are followed regularly by a physician familiar with the condition, ideally in an NF specialty clinic. This often requires a multidisciplinary care approach that may include referrals to an orthopedist, pediatric oncologist, ophthalmologist, dermatologist, radiologist, neuropsychologist, pain management specialist, or plastic surgeon, as needed.

**Is there a test for segmental NF?**

Genetic testing for NF1 and NF2 is usually possible, and is done using a blood specimen to detect the genetic alteration (mutation) responsible for the disorder in a specific person. In principle, for someone with segmental NF, one might expect to see a mutation in some of the blood cells, but not all. Sometimes this is the case when blood is tested. If the mutation is not present in a large quantity of blood cells, however, it may not be possible to detect in blood. Sometimes it is possible to biopsy affected tissue, such as skin or tumor tissue, which can then be tested to detect an NF1 or NF2 gene mutation. A mutation may be present in tissue (and not in blood) due to the mosaic distribution of the mutation throughout different cell types. Genetic testing is usually not necessary to establish a diagnosis of NF, including segmental NF. It can be helpful in cases where the diagnosis is uncertain. If genetic testing is done, it is important that the results are interpreted by a physician or genetic counselor who have experience in interpreting and explaining information obtained from genetic testing.
What are the genetic implications of segmental NF?

Typically a person with segmental NF is the first to be affected in his or her family; one does not expect to see signs of the disorder in either parent. This is because the NF mutation occurred after conception, and was not present in the sperm or egg cell that formed that person. Therefore, it is unusual for parents of a child with segmental NF to have another child with segmental NF or with NF affecting the entire body.

A person with segmental NF may be at risk of passing along the NF mutation to a child. This would be the case if germ cells – sperm or egg cells – carry the mutation. This is difficult to predict, but has been seen in some patients. The risk of transmitting NF could be as high as 50% if all germ cells carry the mutation, could be lower if only some do, or could be zero if the mutation is not in the germline. Sometimes the mutation can be detected in a sample of sperm from a male, but it is difficult to detect the mutation in eggs from a female. It is important to realize that, if a mutation is passed on, it will be present in all of the cells of the child. Therefore, the child will have “full” NF1 or NF2, not segmental NF.

Understanding these recurrence risks can be complicated, and you are encouraged to meet with a genetic counselor to talk about risks to pass NF on to an offspring. Also, in some cases, prenatal testing options may be available.
How can I learn more?

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