



## **Information about localised, segmental or mosaic Neurofibromatosis type 1 (NF1).**

**Localised** Neurofibromatosis, **segmental** Neurofibromatosis or **mosaic** Neurofibromatosis are terms used to describe a person where the signs for NF1 are limited to a particular area of their body. Localised, segmental and mosaic are words that mean the same in this case. The area of the body affected may be just a small strip of skin or as big as a large "segment" of the body. Within these areas are the characteristic signs for NF1; outside them there are no signs at all. That area is unaffected by NF1. Usually the appearance of the skin in the affected area is such that the diagnosis can be easily made without special tests.

In this factsheet we shall just refer to this type of NF1 as "segmental" NF1. Your doctor may refer to it as "localised" or "mosaic" NF1. In order to be clear, we shall call the more usual form of NF1 (when the signs are present over the entire body) "generalised" NF1.

Segmental NF1 is much rarer than "generalised" NF1. It affects 1 in 36000 people compared to 1 in 2500 for the usual form of NF1. Mostly segmental NF1 causes few health problems. The chance of a parent with segmental NF1 having children with NF1 is low.

### **Why does segmental NF1 occur?**

Segmental NF1 arises from a genetic process called mosaicism. Mosaicism can be explained as a situation where the body contains a mixture of cells. Some cells will contain the correct genetic information. Other cells will have a change in the genetic information. The cells that have the changed information in this instance will lead to that area of the body having the changes associated with NF1.

If you think of mosaic tiles on a floor having a mix of patterns, someone with mosaic/segmental/localised NF1 will have a mixture of cells: some normal and some with the gene change.

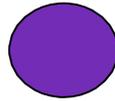
### **How has this happened?**

Our body is made up of cells. The very first cell is created when the sperm

(from the man) fertilises the egg (from the woman). This single cell contains a complete set of instructions that tells the cell how to behave. These instructions will make the person we become – a bit like the ingredients in a cake.

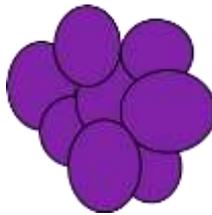
When a baby is born with NF1, the gene misprint (gene fault) that causes NF1 occurs at the moment of conception. So the very first cell created when the sperm fertilises the egg has the genetic misprint for NF1.

*Fertilised cell with the NF1 misprint*



As that single cell divides, first into 2 and then into 4 and so on, the genetic instruction or “code” is copied at each step of the division process. The complicated genetic information is “photo-copied” into all the cells that are formed. If the developing baby (embryo) has NF1, then every cell in their body will carry the NF1 misprint.

*Every cell of this embryo has the NF1 misprint*

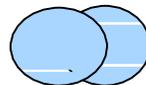


In segmental NF1 the misprint occurs **later** in the process of the cells dividing.

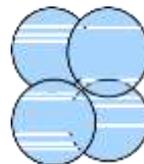
*This fertilised cell contains all the genetic information. It does not have the NF1 misprint*



*The cell divides into 2. All the information is correctly copied*



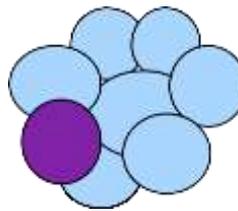
*The cells divide again. None of the cells has a misprint at this stage of development of the embryo*



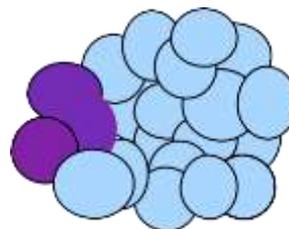
Sometimes the NF1 misprint can occur at a **later stage** in the developing embryo. For example, if the misprint occurs at a stage in the development of the embryo at say 8<sup>th</sup> cell, then only the cells copied from that 8<sup>th</sup> cell with the

NF1 fault will carry the misprint.

*The cells divide again but this time when the genetic information is copied, a misprint occurs. The 8<sup>th</sup> cell carries the misprint for NF1. (This cell is coloured purple to show it clearly).*



*The cells continue to divide. Some will be "normal" cells; a proportion will have the NF1 misprint. (Cells with the NF1 misprint are coloured purple here)*



The stage of development when the misprint occurs dictates the proportion of cells that carry the genetic misprint. The later the misprint occurs in the forming embryo, the smaller the area of the body affected by NF1.

As the developing embryo grows, cells are organised into different specialised groups to form muscle cells, nerve cells, skin cells etc. This organisation of cells occurs according to complicated sets of instructions as genes are switched on and off. A baby born with segmental NF1 will have a mix of cells: some will have the NF1 misprint and others will not. The timing of when the misprint occurred in the organisation of cells determines how segmental NF1 affects each individual.

As the baby grows through childhood and later becomes an adult, the signs of NF1 will be limited to the area of their body where the cells have the NF1 misprint. The signs of NF1 in this segmental form are the same as the more usual type of NF1: they include café au lait patches, freckles and neurofibromas. Careful skin examination may show a clear difference in skin colour within the NF1 affected area compared to the rest of the skin.

NF1 is a very variable condition. Segmental NF1 also varies from one person to another. The risk of developing NF1 linked health complications is much less in this form of NF1. It is still possible for such problems to arise within the area of the body where the cells have the NF1 misprint. For this reason it is important to be aware of unusual symptoms and seek advice from your doctor if problems persist.

### **Can this type of NF1 be passed on to children?**

NF1 can be passed on to children. If you have "generalised" NF1 with the NF1 misprint in every cell, the chance of passing it on to a child is described as 1 in 2, or a 50% risk.

When a parent has segmental NF1 the chance of passing on NF1 is much less: mostly those children will not have NF1. However if they do have NF1, their child will develop the more usual "generalised" form of NF1, with the NF1 genetic miscopy in **every cell of their body**.

The reason this happens is because their parent with segmental NF1 has the NF1 miscopy not just in their skin cells, but in those parts of the body responsible for making eggs or sperm. It is impossible for a doctor to determine this information when they examine someone with segmental NF1. Hence calculating the exact risk of passing on NF1 to any child is not possible. In this kind of situation doctors use what is called an "empiric" risk figure, in other words they make an educated guess. The figure often given to people with segmental NF1 is a 5% or a 1 in 20 chance of passing on NF1.

When a child inherits the NF1 gene from their parent with segmental NF1, that child may have more NF1 related health problems than their parent. However the majority of children born to parents with segmental NF1 will not have NF1 at all.

### **Health checks for people with segmental NF1**

When segmental NF1 is diagnosed in a child, doctors usually recommend regular health checks with a paediatrician to ensure any possible NF1 complication is not overlooked. These checks will be the same as children with "generalised" NF1. As children become adult, if they have just the NF1 skin changes and no other health complications, this group of people may not need further hospital checks.

Some adults with segmental NF1 will need to continue to have regular health checks appropriate to NF1. This will be because they have a health problem that is linked to their diagnosis, for example a lump growing inside their spine. Their health care will be managed by an appropriate hospital specialist. If someone with segmental NF1 develops unusual health changes, it is important to remind doctors investigating those symptoms about the diagnosis in case there is a link.

### **Planning a pregnancy**

Thinking about having children is a major step for most couples. If you have a condition like NF that can be passed on to children, your GP can refer you to a Regional Genetics Service for advice and reliable information to help you to plan for this.

At a genetics clinic you will meet with a doctor who specialises in conditions that can be passed on in families. This is an opportunity to learn more about the condition itself, the risks to children and what tests in pregnancy are currently available.

People with "generalised" NF1 planning a family can consider choices such as testing in pregnancy and pre-implantation genetic diagnosis (PGD) if they wish.

In segmental NF1 such testing is more difficult. A blood test to identify the NF1

miscopied gene is likely to be normal. A further test involving taking cells from within the specific NF1 affected area may be needed.

Genetic testing can be a complicated and lengthy process. For this reason couples who want to consider techniques like this should make contact with the genetics service at a very early stage in their planning, and well before a pregnancy is established. This will enable them to get the best possible advice and information from that service.

**Where can I get more help and information about this type of NF1?** For accurate information about NF1 and segmental NF1 you can ask your GP to refer you to the nearest regional genetics centre. This is an NHS hospital based service.

In addition there are 2 nationally funded Neurofibromatosis Centres that specialise in the diagnosis and management of the different forms of Neurofibromatosis. The two centres are Guy's Hospital in London and St Mary's Hospital in Manchester (St Mary's is the lead centre for segmental NF1 and the laboratory tests are done there).

Patients from outside England can be referred but funding must be agreed before accessing the service. Again you need to discuss this with your GP or specialist doctor.

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**Please seek further information from [www.nervetumours.org.uk](http://www.nervetumours.org.uk), or contact our helpline on the details above.**

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