



# Melanocortin-4-Receptor (MC4R)

Information for patients and families with MC4R deficiency.

**Disclaimer:** This information is for families where there has been a diagnosis of MC4R deficiency. This leaflet may not provide information that addresses your individual health concerns as it is intended for general information only.

## **Melanocortin-4-Receptor deficiency (MC4R deficiency)**

### **What is MC4R deficiency?**

We first described the condition in 1998, at the same time as a French team. We now know that it is the most common genetic cause of weight problems. Many people will not have heard of MC4R deficiency, even many doctors and nurses, but this is beginning to change.

Children with this condition often feel very hungry and are usually overweight from a young age. We have discovered that when people gain weight at a very young age this can be due to a problem with a gene. That is exactly what MC4R deficiency is - a problem in a gene that should normally control your weight. The gene's name is MC4R.



### **How do you get it?**

MC4R deficiency is caused by a gene that doesn't work properly. It is a genetic condition that is present at birth, occurs in both males and females, and causes weight problems with varying degrees of severity.

If you or your child has this gene problem, then you will always have the faulty gene.



### **More about the MC4R gene**

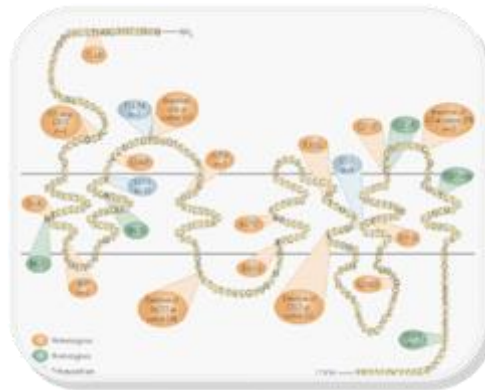
We can inherit a lot of things from our parents, for example the colour of our eyes and our height.

This information is passed down the generations in our DNA.

Our DNA is organised into small blocks called genes which have specific functions. For example, there is a gene for red hair and one for blue eyes and thousands of other genes.

Every gene (including MC4R) has two copies, one copy comes from your mother and the other, from your father.

In MC4R deficiency, one of these genes is faulty and the other gene is normal. Very rarely, a person can inherit two faulty MC4R genes.



### **How can a faulty gene cause a weight problem?**

You can think of a gene as being made up of a string of letters which need to be in the correct order to make sense.

If this happens, the correct term for the faulty gene, is a “mutation “and you can see from the cartoon of the gene, there are many different mutations in the MC4R gene.



The MC4R gene tells a specialised area of our brain, called the hypothalamus, about our energy levels so it can regulate how much we eat and how we use and store calories. It doesn't take much to upset the fine tuning of this system that ultimately regulates our weight.

When the brain senses low energy levels, it sends out hunger signals. When we eat a meal, our body sends signals to the brain telling us we are full. If the MC4R gene isn't working properly, then these signals become confused and a person can feel like they are hungry even if they have eaten quite a bit of food.

### **How common is it?**

It is the commonest gene problem to cause severe weight problems but it is still rare! Estimates of just how many people have a problem with the MC4R gene have changed as the condition has become more recognised. If we look at people with severe weight problems starting in childhood, about 5 children in every 100 have a faulty MC4R gene. In the general population, this figure is lower, about 1 in every 300 people.

**To find out more, look at our website [www.mc4r.org.uk](http://www.mc4r.org.uk)**

### **What does having this gene problem mean for me and my family?**

The MC4R gene is inherited which means that it runs in the family. So, when one individual in the family is diagnosed with MC4R deficiency, there may be implications for parents, brothers & sisters and other relatives. In some families, it may have been the cause of weight problems through several generations.

**“It’s nobody’s fault, just one of those things that can happen”.**

It is important to say that there are many different mutations that have been found in this gene. Sometimes the gene doesn’t work at all, sometimes it is partially faulty and some people can have a milder version of the condition, even within the same family.



### **How do you find out if you have inherited this gene problem?**

You or someone in your family may have been referred to the team in Cambridge for tests into genes that lead to weight problems. Genes can be tested by collecting a DNA sample from a mouth swab or saliva kit or from a blood sample.

Sometimes, finding out that someone in the family has a gene problem, comes as a bit of a shock. Many families of MC4R children tell us that they always knew that there was something wrong, they have often been telling that to Doctors for years! Many of you say it is a relief to get a diagnosis, as at least then there is a reason behind the difficulties that you and your family often experience. It can be helpful to have letters from us to help to guide schools, employers and health care professionals.

### **What does it mean for me and my family?**

Thanks to the help of many of our patients and families who have to come to Cambridge to help with our research, we now know a great deal about what happens when this gene is faulty.

We know that children with this condition are often constantly hungry, never feel satisfied after a meal and in some cases may steal food or even eat things that aren’t food, such as paper. This is not their fault, their brain is telling them that they are hungry all the time.

We also know that people with MC4R deficiency do not use up the fat that they eat in the same way as other people. This means that they will store fat and gain weight far more easily even if they eat

the same food as someone else. They often find it more difficult to lose weight than people without this gene problem.

Children with MC4R deficiency are often tall for their age and may have higher levels of the hormone insulin in their blood (this can contribute to their tallness). Patients with this condition also have more muscle and bigger bones. We think this is probably a good thing.

Many patients with MC4R deficiency seem to have a lower blood pressure and a lower cholesterol than people of the same weight that do not have a MC4R gene problem.

The more we find out about MC4R deficiency, the closer we get to finding treatments, not only for MC4R patients but hopefully for others too. So a big thank you to all those who have helped us over many years.

### **Is there any treatment?**

Recently Semaglutide (Wegovy) has been approved for the treatment of obesity in adults and this treatment is known to be effective in patients with MC4R deficiency. Further drugs are currently in clinical trials and we will keep our website updated when these become available.

**One of our MC4R patients has set up a facebook "[MC4R patient and family support group](#)" It is a "Private" group so if you are interested, you will have to request to join the Group. All posts are private and can only be seen by other members.**

### **What is the outlook?**

Typically, children with MC4R deficiency will be hungry from a very young age and will continue to gain weight during childhood. By knowing that they have a gene problem, it may help everyone to understand that it is not because they are "naughty" or "greedy" but that they genuinely feel constantly hungry and want food.

Most patients will remain severely overweight as adults and will have difficulty losing weight via conventional diets. This means that even when your diet is controlled very carefully, you will struggle to lose weight because the normal mechanisms for losing weight by burning stored fat, require both MC4R genes to be normal. Some adults with this condition do lose weight after bariatric surgery.

Patients with MC4R are at risk of the conditions which generally accompany being overweight. This may include Type 2 Diabetes and joint problems.

### **Who can you contact if you have questions?**

You can contact us by email or phone. We will try to get back to you as soon as we can. We want to be able to let you know of any new findings and if you are willing to help us, we will let you know about any new studies.

Visit MC4R website at [www.mc4r.org.uk](http://www.mc4r.org.uk) to learn more about our work.

Or email us at [cuh.genetics.of.obesity@nhs.net](mailto:cuh.genetics.of.obesity@nhs.net) to stay up-to-date with what we're doing and find out how you can get involved.