INFORMATION FOR PATIENTS WITH MATURITY-ONSET DIABETES OF THE YOUNG CAUSED BY A CHANGE IN THE HEPATIC NUCLEAR FACTOR 1 ALPHA GENE (HNF1A)

What is HNF1A?

HNF1A is a gene which acts as a switch that turns on and off other genes in the body. Changes in the *HNF1A* gene cause diabetes by lowering the amount of insulin that is produced by the pancreas. It allows insulin to be produced normally in childhood but the amount of insulin reduces as you get older. *HNF1A* is one of a group of familial types of diabetes called maturity onset diabetes of the young (MODY). *HNF1A* accounts for 70% of MODY cases.

What can we say about diabetes caused by changes in *HNF1A*?

People with a change in the *HNF1A* gene are likely to develop diabetes. Typically, they do not have diabetes in childhood but develop diabetes during adolescence or early twenties, although some people may not be diagnosed until middle or old age. There is often an increasing need for treatment as the affected individual gets older and so most people will go on to need either tablets or insulin to stop their blood glucose becoming too high. This progression may take place over many years.

It is important to keep blood glucose controlled in this type of diabetes as it can lead to diabetic complications such as damage to the small blood vessels in the eyes and kidneys. This can be prevented if blood glucose levels are kept well controlled. The risk of coronary heart disease is also raised in HNF1A diabetes even though levels of the 'healthy' cholesterol HDL are usually high, so early treatment (from the age of 40) with cholesterol lowering medications to protect the heart is recommended. People with changes in the *HNF1A* gene often pass increased amounts of glucose in their urine so may have glucose detected on urine testing when their blood glucoses are normal.

How is HNF1A diabetes treated?

Individuals with HNF1A diabetes are often particularly sensitive to the blood glucose lowering effects of a group of drugs called sulphonylureas. Sulphonylureas include drugs like Gliclazide, Glipizide, Glibenclamide and Tolbutamide and work by stimulating the pancreas to produce insulin. Early after the diagnosis of diabetes control is often better with sulphonylurea tablet treatment than with insulin, though as diabetes progresses with time insulin may be needed in later life. People with HNF1A diabetes who have been taking insulin from diagnosis prior to a genetic test which confirmed a diagnosis of HNF1A diabetes may be able to stop insulin and convert to sulphonylurea tablet treatment instead.

Should HNF1A patients look after their diabetes differently?

No. One thing that our research shows is that keeping physically active and slim helps to keep the blood glucose controlled. This is no different from the advice we would give to anybody with diabetes.

Does this result mean that my diabetes is the same as my parent who had diabetes?

It is very likely that a change in the *HNF1A* gene was also present in one of your parents and would have caused them to have diabetes as well. This does not mean that your diabetes will be identical to theirs and there can be considerable variation within the family. In particular, just because a parent or other family member has had ill health resulting from their diabetes, this does not mean that you will have a similar problem, particularly if your blood glucose is well controlled.

How does this affect other family members?

Approximately half the children born to a parent with HNF1A diabetes will develop diabetes themselves. This is due to the 50% chance of the affected gene being passed on from a parent at conception. Children and brothers and sisters of people with HNF1A diabetes who have inherited the same change in the *HNF1A* gene have a 63% chance of developing diabetes by the age of 25 years and 96% chance by the age of 55 years. Family members of a patient known to have HNF1A diabetes should be aware of the symptoms of diabetes and have their blood glucose measured if they are concerned that they may have it. Predictive genetic testing (to see if they have inherited the same change in the gene) is also possible – please see the section on predictive genetic testing on our website.

Further Information

Research Articles**:**

R Murphy, S Ellard, AT Hattersley (2008) Clinical implications of a molecular genetic classification of monogenic beta cell diabetes. Nature Clinical Practice Endocrinology and Metabolism 4: 200-213.

Shepherd M, Pearson ER, Houghton J, Salt G, Ellard S, Hattersley AT (2003)
No deterioration in glycaemic control in HNF-1alpha maturity-onset diabetes of the young following transfer from long-term insulin to sulphonylureas.
Diabetes Care 26: 3191-3192.

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