INFORMATION FOR PATIENTS WITH A HIGH BLOOD SUGAR DUE TO A CHANGE IN THE GLUCOKINASE GENE

What is glucokinase?

Glucokinase (*GCK*) is a gene which plays an important role in recognising how high the blood glucose is in the body. It acts as the "glucose sensor" for the pancreas, so that when the blood glucose rises, the amount of insulin produced also increases. This means that the blood glucose does not become too high if glucokinase is functioning normally. Changes in the *GCK* gene can lead to increases in blood glucose and affected people may be diagnosed with diabetes although this rise in blood glucose is mild and usually does not need treatment. Glucokinase diabetes is one of the familial diabetes types that together are often called MODY (maturity onset diabetes of the young).

What does it mean if there is a change in the GCK gene?

If there is a change in the *GCK* gene this means that it works slightly differently so that the blood glucose is "reset" at a higher level than in people without this change. In people without a change in *GCK*, the blood glucose is usually around 5.5mmol/L but in people with a change in the glucokinase gene, the fasting blood glucose is typically between 5.5 and 8mmol/L. A diagnosis of diabetes is often made if the fasting blood glucose is over 7mmol/L. The blood glucose is typically raised from birth and is stable throughout life. Unlike other types of diabetes the increase in blood glucose after eating is usually small. A glucose tolerance test may be performed to identify if an individual has diabetes. With *GCK* gene changes the rise in blood glucose during this test is usually small (less than a 3mmol/L increase in 70% of patients at 2 hours).

How is glucokinase diabetes treated?

Because the rise in glucose that occurs with changes in the *GCK* gene is mild there are usually no symptoms so it is often only identified during routine screening (for example during pregnancy). Complications of diabetes are very rare therefore usually no treatment is needed. If diabetes treatment is started it may make very little difference to blood glucose levels as the body will keep trying to maintain the blood glucose at the raised level.

The presence of a change in the *GCK* gene is most significant in pregnancy. If there is evidence that the baby is growing more quickly than usual on antenatal ultrasound scans mothers may be treated with insulin to try to control blood sugars and hence the baby's growth however there is currently debate about the role of insulin in this situation.

It is possible for an individual with a change in the *GCK* gene to develop other types of diabetes that require treatment. Patients have the same risk of developing Type 2 diabetes as other members of the general population. Type 2 diabetes is common in older people especially if they are overweight and can need tablet or insulin treatment.

How does this affect other family members?

Approximately half the children born to a parent with a change in the *GCK* gene will inherit the same change leading to a mildly raised level of blood glucose throughout life. This is due to the 50% chance of the affected gene being passed on from a parent at conception. Family members of a patient known to have GCK MODY should be aware they may have inherited the same genetic change and may have their fasting blood glucose measured if they are concerned that they may have it, particularly if they are planning pregnancy as the raised blood glucose may need treatment at this time.

Further Information

Research Articles**:**

Clinical implications of a molecular genetic classification of monogenic beta cell diabetes. R Murphy, S Ellard, A Hattersley. Nature clinical practice endocrinology and metabolism 2008 Apr;4(4):200-13.

Different genes, different diabetes: lessons from maturity-onset diabetes of the young. Stride A, Hattersley AT. Ann Med. 2002;34(3):207-16.

Prevalence of vascular complications among patients with glucokinase mutations and prolonged, mild hyperglycemia. Steele AM, Shields BM, Wensley KJ, Colclough K, Ellard S, Hattersley AT. JAMA. 2014 Jan 15;311(3):279-86.

Cross-sectional and longitudinal studies suggest pharmacological treatment used in patients with glucokinase mutations does not alter glycaemia. Stride A, Shields B, Gill-Carey O, Chakera AJ, Colclough K, Ellard S, Hattersley AT. Diabetologia. 2014 Jan;57(1):54-56.

Use of HbA1c in the identification of patients with hyperglycaemia caused by a glucokinase mutation: observational case control studies. Steele AM, Wensley KJ, Ellard S, Murphy R, Shepherd M, Colclough K, Hattersley AT, Shields BM. PLoS One. 2013 Jun 14;8(6):e65326.

Chakera AJ, Steele AM, Gloyn AL, Shepherd MH, Ellard S, Hattersley AT. Recognition and Management of Individuals with Hyperglycemia Because of a Heterozygous Glucokinase Mutation. Diabetes Care (2015) 38(7):1383-1392.

Contact for advice/clinical enquiries**:**

Maggie Shepherd 01392408160 (mornings) or email M.H.Shepherd@exeter.ac.uk
Anna Steele 01392408173 or email annasteele@nhs.net

Website:
www.diabetesgenes.org