Information for patients with a disease-causing variant in the Hepatocyte Nuclear Factor-1 Beta (*HNF1B*) gene

What is Hepatocyte Nuclear Factor-1 Beta (*HNF1B*)?

HNF1B is a gene which acts as a switch to turn other genes on and off in the body. It is involved in the development of several organs in the body including the kidneys, pancreas, reproductive tract, and liver. People with a disease-causing variant in the *HNF1B* gene can have a variety of problems associated with these organs. This is sometimes called the "Renal Cysts and Diabetes or RCAD syndrome" because these are the most common features.

How do variants in *HNF1B* affect the kidneys?

The kidney is the most common organ to be affected in people with a variant in the *HNF1B* gene. HNF1B is important for the control of kidney development before a baby is born. Variants in the *HNF1B* gene can affect this process to different degrees. The most common finding is cysts (fluid filled swellings) in the kidneys. These are usually seen when an ultrasound scan is performed to look at the size, shape and structure of the kidneys. Other features associated with a variant in the *HNF1B* gene include small kidneys or the presence of only one kidney which may be of normal or abnormal shape. Sometimes abnormalities in the kidneys of a baby with a variant in the *HNF1B* gene are noticed before the baby is born when the mother is having an antenatal scan. The abnormalities in the kidneys have a variable effect on how well the kidneys work. Some people are only mildly affected and may have cysts in their kidneys but they work normally. Other people may be more severely affected and their kidneys may fail in which case artificial kidney treatment (dialysis) or a kidney transplant is required. In rare cases the kidneys fail to develop at all which may lead to the death of a baby in the womb.

What about *HNF1B* and diabetes?

Variants in the *HNF1B* gene are associated with an increased risk of developing diabetes. Diabetes is the second most common problem in people with a variant in the *HNF1B* gene after kidney abnormalities. However not all people with a variant in the *HNF1B* gene develop diabetes. Diabetes can develop at any age but often develops in adolescence or young adulthood and sometimes in pregnancy. Patients with an *HNF1B* variant can be affected with diabetes but have no clinical signs or symptoms of renal disease. Diabetes caused by variants in *HNF1B* is more commonly treated with insulin injections although it may be possible initially to use diet or tablets.

Some people with variants in the *HNF1B* gene also have a pancreas that is smaller than usual. This can be picked up on different types of scans (CT, MRI and sometimes ultrasound). The pancreas is an organ found in the abdomen that produces important enzymes and hormones (including insulin) to help break down food. If people are not

making enough of these enzymes, this can cause loose stools and unintentional weight loss because they can't digest their food properly. However, they can be replaced by taking tablets with their meals.

What about *HNF1B* and uterine abnormalities?

Women with a variant in the *HNF1B* gene can have abnormalities of the reproductive tract, especially uterine abnormalities. This usually means that the uterus is a different shape or there may be a double uterus. These problems may be picked up on an ultrasound scan. It is possible for a woman with a uterine abnormality caused by a variant in the *HNF1B* gene to have a successful pregnancy.

What else can variants in the *HNF1B* gene affect?

Some people with variants in the *HNF1B* gene have mild abnormalities on blood tests of liver function, or an abnormal looking liver when scanned. However this does not seem to cause significant liver disease.

Some people, including women and young adults, are prone to attacks of gout and high levels of uric acid can be found in the blood. This is a result of the kidneys being unable to remove uric acid from the body as efficiently as they should. It is possible to take tablets to prevent attacks of gout.

Some people have low levels of magnesium on blood tests. However, this does not usually cause any symptoms and only a small number of people will need to take magnesium supplements.

Does this result explain why other members of my family have kidney problems and diabetes?

If other members of your family are known to have kidney abnormalities such as cysts and diabetes it is likely that they also carry the same variant in the *HNF1B* gene. The genetic variant can pass from generation to generation, although sometimes it occurs as a new variant (referred to as a *de novo* variant) so there may be no-one else in the family affected. The range and severity of the abnormalities often varies widely within one family.

Will this affect my children?

We know that anyone who has a variant in the *HNF1B* gene has a 50% chance of passing this on to their children. It is important to remember that the effects can vary widely; detailed antenatal scanning particularly of the kidneys can be helpful in detecting abnormalities.

Can my family be tested?

It is possible to test other family members for the familial *HNF1B* variant, but it is important to consider discussing this first with a genetic counsellor.

What do I do if I want to know more?

If you would like to know more, the best thing to do is ring between 0900 and 1700 to arrange to talk to Dr Coralie Bingham on 01392-406366. Alternatively you can write with any questions to the following address:

Dr Coralie Bingham
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There are also two websites with further information: **www.diabetesgenes.org** and **www.rarerenal.org**.