MODY

Monogenic diabetes, or **M**aturity-**O**nset **D**iabetes of the **Y**oung

What is monogenic diabetes?

- Monogenic diabetes, or **M**aturity-**O**nset **D**iabetes of the **Y**oung (MODY) is a rare form of diabetes. It is different from Type 1 Diabetes and Type 2 Diabetes.
- MODY is caused by a mutation in a single gene, and therefore can be passed from parents to children. There are now more than 14 different gene mutations that lead to different forms of MODY.
- Like other forms of diabetes, MODY can affect how the body produces insulin. Insulin is made in the pancreas and allows the cells in the body to take up and use sugar. Problems with insulin production can lead to high levels of sugar in the blood and symptoms of diabetes.

Key features of MODY:

- Parent with diabetes (and often a grandparent)
- Age at diagnosis typically less than 25-30 years old
- May or may not require insulin

How do you get MODY?

- MODY is inherited in an Autosomal Dominant pattern. This means that when a person has it, their child will have a 50% chance of getting the mutation as well. So in most cases, people develop MODY by getting the gene mutation from one of their parents.
- You CAN have obesity and have MODY, but you did not develop MODY because of your weight.

What if someone with MODY does not have parents with MODY?

- Individuals with MODY may be the first one in their family to develop the mutation. They can then pass it to their children 50% of the time.
- It is also possible that one of their parents may have MODY, but has never been tested or diagnosed. Most women are tested for diabetes during pregnancy so if the individual's mother had gestational diabetes there is a chance that she actually has MODY. If not, it may have come from the father's side and he may never have been tested.

How do you test for MODY?

- MODY is still a very rare form of diabetes, so your provider should be able to help with the decision of whether or not to test.
- A genetic test by blood draw can look for the genetic mutations. Genetic testing is frequently offered to family members of those with MODY since it often runs in families.

Why is understanding your MODY diagnosis is so important?

- Patients are often told they have Type 1 or Type 2 diabetes before they are actually diagnosed with MODY. However, MODY is treated differently from type 1 or type 2 diabetes.
- As a result, the correct diagnosis ensures better treatment for your child.
- You should understand what type of diabetes your child has and should share this information with your child's healthcare team to familiarize them with the condition. It helps to keep a picture of the results on your phone to show to their providers.

- Consider asking about getting other relatives tested for MODY as well.

Most Common MODY Types

MODY-1

Genetic Defect	Mutation in HNF-4 alpha (HNF4α) gene.
Frequency	5-10% of MODY cases.
Clinical Presentation	May have had large birth weight or low blood sugars in the newborn period.
Treatments(s)	• Oral sulfonylurea (Glyburide/Glimepiride/Glipizide). • May need insulin during illness or pregnancy.
Complication(s)	Patients **are at risk for complications** of diabetes.

MODY-2

Genetic Defect	Mutation in Glucokinase gene which helps set the level of blood sugar at which your body will increase insulin production.
Frequency	30-60% of MODY cases.
Clinical Presentation	Higher fasting blood sugar level that does not progress over time.

Treatments(s)	▪ Usually no treatment is needed. ▪ May need insulin during illness or pregnancy.
Complication(s)	Patients are at low risk for complications of diabetes.

MODY -3

Genetic Defect	Mutation in HNF-1 alpha (HNF1α) gene.
Frequency	30-60% of MODY cases.
Clinical Presentation	Insulin production does not increase appropriately when blood sugars rise.
Treatments(s)	• Oral sulfonylurea (Glyburide/Glimepiride/Glipizide). • May need insulin during illness or pregnancy.
Complication(s)	Patients **are at risk for complications** of diabetes.

MODY-4

Genetic Defect	Mutation in PDX-1 (also called IPF-1) gene
Frequency	Uncommon
Clinical Presentation	Insulin production does not increase appropriately when blood sugars rise.
Treatments(s)	Usually start with oral sulfonylureas (Glyburide/Glimepiride/ Glipizide) but may eventually need insulin.
Complication(s)	Unclear if patients are at risk.

MODY-5

Genetic Defect	Mutation in HNF-1 beta (HNF1β) gene
Frequency	< 5% of diagnosed MODY cases.
Clinical Presentation	▪ Associated with renal cysts in the kidney, kidney disease, and other rare congenital anomalies/malformations. ▪ Early diabetes onset may occur for 50% of affected patients.
Treatments(s)	Usually unresponsive to oral medications and require insulin.
Complication(s)	Patients are at risk of microvascular complications.