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MONOGENIC DIABETES

What is monogenic diabetes?

- Prediabetes or diabetes that is caused by a single genetic abnormality
- Includes MODY (maturity-onset diabetes of the young), neonatal diabetes, and syndromic forms

How prevalent is monogenic diabetes?

- Estimated to affect ~2-5% of those diagnosed with diabetes at <35 years of age, 0.4% of diabetes cases overall

How do I know if my patient has monogenic diabetes?

- **Clinical features can give us a suspicion**
 - If you think your patient doesn't appear to have typical Type 1 Diabetes or Type 2 Diabetes, that is a good start.
 - See [Table 1](#) for specific clinical features
- **Genetic testing is the only way to know for sure**
 - Many universities and commercial genetic testing companies offer testing for monogenic diabetes

Why does identifying patients with monogenic diabetes matter?

- Once the type of monogenic diabetes is known, there may be *treatment implications* such as changing to specific medications, coming off insulin and/or all medications
- Answers their question – 'why did I get diabetes?'
- Helps us decide what other types of testing to do (such as checking the liver, kidneys, etc)
- There are typically *family member implications*
 - E.g., Autosomal dominant forms: 50% chance of passing to children

Resources on monogenic diabetes:

- University of Chicago Monogenic Diabetes Program: <https://monogenicdiabetes.uchicago.edu>
- Expert consultation, letter of support templates for insurance approvals, educational materials, research studies including longitudinal Registry of known monogenic diabetes and (free) research-based genetic testing for those who qualify
- Participants or clinicians may email us at: monogenicdiabetes@uchicago.edu
- MODY Testing Guide for Providers – <http://bit.ly/MDRAP-Resources>
- Monogenic Diabetes Research & Advocacy Consortium: <https://www.mdrac.org>
- Wolfram Syndrome International Registry and Clinical Study: <https://wolframsyndrome.wustl.edu>
- Find a genetic counselor: <https://www.nsgc.org/page/find-a-genetic-counselor>
- MODY probability calculator: <https://www.diabetesgenes.org/exeter-diabetes-app/ModyCalculator>

Table 1. Clinical features that may be suggestive of monogenic diabetes

- Anyone diagnosed ≤6-12 months of age
- Diagnosed ~1-35 years of age with the following features:
 - Does not fit with 'typical' Type 1 Diabetes:
 - Negative for diabetes autoantibodies
 - Unusually low insulin requirements when 3+ years out from diagnosis
 - 2+ linear generations of family members with similar diabetes, diagnosed <35 years of age
 - Does not fit with 'typical' Type 2 Diabetes
 - No evidence of metabolic syndrome – no dyslipidemia, no hypertension, no acanthosis
 - Lack of obesity (BMI percentiles <95th percentile for children, or BMI <30 kg/m² for adults) – *NOTE: Having a BMI in the obese range does not rule out the possibility of monogenic diabetes. Consider the whole clinical picture.*
 - 2+ linear generations of family members with similar diabetes, diagnosed <35 years of age
- Other features that may be suggestive:
 - Strong family history of diabetes and kidney cysts, abnormally shaped kidneys, abnormally shaped genitourinary tract
 - Diabetes and liver adenomas
 - Mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes (MELAS) or maternally-inherited diabetes and deafness (MIDD)

OTHER RARE AND ATYPICAL FORMS OF DIABETES

What is atypical diabetes?

- Hyperglycemia that is not 'typical' Type 1, not 'typical' Type 2, and not known forms of monogenic diabetes (negative genetic testing)
- Examples of atypical diabetes include:
 - Type 2 Diabetes diagnosed before puberty, lean Type 2 Diabetes
 - Strong family history of diabetes with early onset (but not monogenic diabetes)
 - Non-progressive or rapidly progressive
 - Low insulin requirements (<0.5 u/kg/day)
 - Cyclical, periods of remission
 - Lean Polycystic Ovarian Syndrome (PCOS) with diabetes
 - Lean gestational diabetes
 - Ketosis Prone Diabetes – subtypes A-B- or A-B+ (unprovoked DKA at diagnosis) (A: Antibody status, B: Beta cell function)

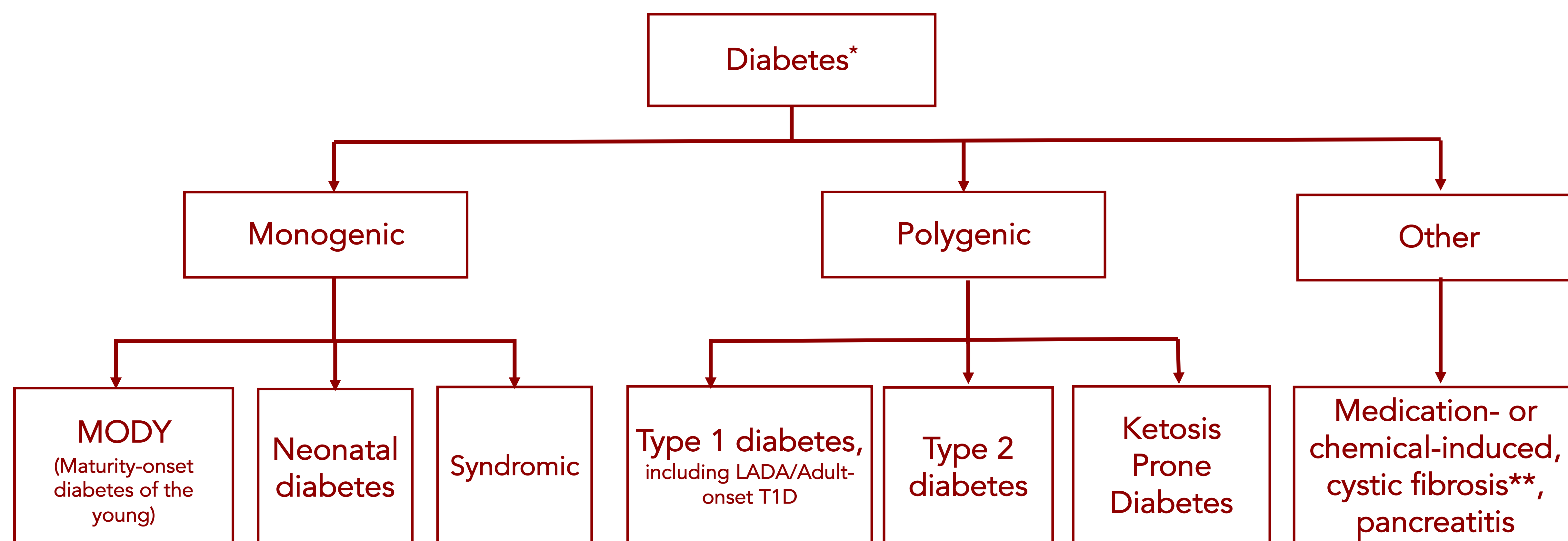
Resources on other forms of atypical diabetes:

- RADIANT (Rare and Atypical Diabetes Network) research study – patients may sign up at www.atypicaldiabetesnetwork.org

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Figure 1. Diabetes classification through a genetics lens



*This figure does not necessarily depict all types of diabetes.

**Cystic fibrosis-related diabetes (CFRD) is listed under 'Other' and not 'Monogenic' because although CF is caused by genetic mutations, the mechanism is complex.