MAND Lab Handout #5: Glucose Growth Hormone Testing

IMPORTANT DISCLAIMER: These handouts are based on emerging research and mechanistic reasoning from animal models and cell studies — no MAND-specific clinical testing guidelines currently exist. The metabolic framework is hypothetical but grounded in published molecular data. Results need to be interpreted by providers familiar with both MAND and metabolic medicine.

Understanding Glucose Growth Hormone Testing for MAND

What is this testing for?

Research in animal models of MAND has shown that MBD5 plays a role in controlling blood sugar and growth. Specifically, animals missing MBD5 showed:

- Enhanced insulin sensitivity (the body responds too strongly to insulin)
- Episodes of low blood sugar (hypoglycemia)
- Reduced growth hormone and IGF-1 (a hormone important for growth)

These changes could contribute to fatigue, low energy, poor growth, and episodes of irritability or lethargy — especially if blood sugar drops too low.

Tests that may be ordered:

- Fasting glucose and insulin: Measures blood sugar and the hormone that controls it. In MAND, blood sugar may be on the low side, and the body may be overly sensitive to insulin.
- IGF-1 (Insulin-like Growth Factor 1): This hormone is controlled by growth hormone and is important for growth and development. Low levels may contribute to short stature and fatigue.

- IGFBP-3 (IGF Binding Protein 3): Measured alongside IGF-1 to give a more complete picture of the growth hormone system.
- Hemoglobin A1c (HbA1c): This test shows the average blood sugar over the past 2–3 months. A low HbA1c could indicate chronic low blood sugar episodes.
- Continuous glucose monitoring (CGM): In some cases, the provider may recommend wearing a small sensor on the skin for 1–2 weeks that continuously tracks blood sugar. This can catch low blood sugar episodes that happen between meals, during sleep, or during illness — times when a single blood test would miss them.

Important note about IGF-1 and growth hormone deficiency:

A low IGF-1 level alone CANNOT diagnose growth hormone deficiency. Research has shown that IGF-1 has limited accuracy as a standalone diagnostic test — in one large study, IGF-1 had only 68.5% sensitivity and 41.7% specificity for growth hormone deficiency, meaning it misses many children who truly have the condition and also falsely flags many who do not. IGF-1 levels can be affected by many factors beyond growth hormone, including nutrition, age, puberty status, and chronic illness.

If IGF-1 is low, the next step is referral to a pediatric endocrinologist for growth hormone stimulation testing. This involves giving a medication (such as arginine, clonidine, or glucagon) that should trigger the body to release growth hormone, and then measuring whether the growth hormone response is adequate. Most guidelines require at least one — and often two — stimulation tests to confirm growth hormone deficiency before treatment can begin.

In MAND specifically, a low IGF-1 could reflect true growth hormone deficiency (as seen in the animal model), but it could also reflect the metabolic stress and nutritional factors associated with the condition. Stimulation testing is essential to distinguish between these possibilities.

What do the results mean?

If testing shows low fasting glucose, low IGF-1, or a low HbA1c, it may mean:

- The body is using up blood sugar too quickly

- Growth hormone signaling is impaired
- Episodes of fatigue or behavioral changes may be related to blood sugar drops

Possible interventions may include:

- More frequent meals and snacks with balanced protein, fat, and complex carbohydrates
- Avoiding long fasting periods (especially overnight)
- Bedtime snacks with slow-digesting nutrients
- Referral to a pediatric endocrinologist for growth hormone stimulation testing if IGF-1 is low or growth velocity is poor

When to seek urgent care:

If your child shows signs of low blood sugar — shakiness, excessive sleepiness, confusion, pale skin, sweating, or difficulty waking — check blood sugar if a glucometer is available and contact the provider. If blood sugar is below 60 mg/dL or symptoms are severe, seek emergency care.

How to prepare:

- Fasting for 8–12 hours is required for glucose and insulin testing
- IGF-1 and IGFBP-3 do not require fasting
- HbA1c does not require fasting
- For CGM, the provider will give specific instructions for sensor placement

References:

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- Yuen KCJ, et al. "AACE/ACE Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning From Pediatric to Adult Care." Endocrine Practice. 2019;25(11):1191-1232.