

MAND Lab Handout #1: Energy Metabolism Mitochondrial Function Tests

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 Energy Metabolism Mitochondrial Function Testing for MAND

What is this testing for?

Every cell in the body has tiny power plants called mitochondria that turn food into energy. Research has shown that in MAND (MBD5-associated neurodevelopmental disorder), a specific change happens: a protein called PDK1 is reduced, which causes the body to push too much fuel (pyruvate) into the mitochondria too quickly. This can overload the energy-making system and lead to fatigue, low energy, and muscle weakness.

These tests check how well the energy system is working.

Tests that may be ordered:

- Plasma lactate and pyruvate (with a ratio): These measure the basic fuel molecules in the blood. In many mitochondrial conditions, lactate goes up. In MAND, lactate may look normal or even low because the body is using up pyruvate too fast — so a "normal" lactate does NOT rule out a problem.
- Plasma alanine: Alanine is made from pyruvate. In MAND, alanine may be LOW (not high, as in other mitochondrial conditions) because pyruvate is being consumed too quickly.
- Urinary organic acids: This is a urine test that looks at many different waste products from energy metabolism. Key things to look for include:

- Isocitric acid — may be elevated, which can indicate the energy cycle is backed up
- Krebs cycle intermediates (citric acid, succinic acid, fumaric acid) — these show how the energy cycle is functioning
- Lactic acid in urine — may be elevated even when blood lactate is normal
- Ethylmalonic acid — can indicate problems with the energy chain
- 3-Methylglutaconic acid — a marker of mitochondrial membrane stress
- Plasma acylcarnitine profile: Checks whether fat is being properly burned for energy. Mitochondrial problems can cause a backup in fat processing.
- FGF21 and GDF15 (blood tests): These are newer, more sensitive markers of mitochondrial stress. They may be elevated even when lactate is normal.
- D-Lactic acid: Elevated levels may indicate gut bacteria are producing excess acid, or that a detoxification pathway (which uses glutathione) is under stress.

What do the results mean?

In MAND, the pattern is often different from what doctors typically expect with mitochondrial problems:

- Lactate may be NORMAL (this does not mean the mitochondria are fine)
- Alanine may be LOW (the opposite of what textbooks say)
- Isocitrate may be HIGH (this is a better marker of the energy problem in MAND)
- D-Lactate may be HIGH

If these tests show abnormalities, it may help guide nutritional support strategies such as specific B vitamins, CoQ10, or other supplements that support mitochondrial function.

How to prepare:

- Fasting may be required for some blood tests — ask the ordering provider
- Urine should ideally be a first morning void
- Avoid strenuous exercise the day before testing, as this can affect results
- Bring a list of all current supplements and medications

References:

- Meguro-Horike M, et al. "Haploinsufficiency of MBD5 and MBD6 Impairs Mitochondrial Respiration Through Chromatin-Mediated Gene Regulation." *Biochemical and Biophysical Research Communications*. 2026;800:153288.
- Du Y, et al. "The Essential Role of Mbd5 in the Regulation of Somatic Growth and Glucose Homeostasis in Mice." *PLoS One*. 2012;7(10):e47358.