

MAND Metabolic Lab Quick Reference Guide for Physicians

IMPORTANT DISCLAIMER: Based on emerging research and mechanistic reasoning from animal/cell models. No MAND-specific clinical testing guidelines currently exist. This framework is hypothetical but grounded in published molecular data (Meguro-Horike et al., BBRC 2026; Tao et al., Br J Haematol 2014; Du et al., PLoS One 2012).

MAND (MBD5-Associated Neurodevelopmental Disorder)

Recommended Metabolic Lab Panel — Quick Reference

FASTING REQUIRED for panels marked with (F). Hold iron supplements 24–48 hrs before iron panel. Hold CoQ10 supplements before testing per clinical judgment.

1. ENERGY METABOLISM / MITOCHONDRIAL FUNCTION
2. Plasma lactate and pyruvate (with L:P ratio) (F)
3. Plasma alanine (F) — expect LOW (not high) due to ↓ PDK1 shunting pyruvate into mitochondria
4. Urinary organic acids (first morning void) — key markers:
5. Isocitric acid (may be ↑ — better marker than lactate in MAND)
6. Krebs cycle intermediates (citric, succinic, fumaric, malic acid)
7. Lactic acid, D-lactic acid
8. Ethylmalonic acid
9. 3-Methylglutaconic acid
10. Plasma acylcarnitine profile
11. FGF21 and GDF15 — sensitive mitochondrial stress markers (may be ↑ when lactate is normal)

12. AMINO ACID PROFILE

13. Comprehensive plasma amino acids (F, minimum 4 hrs) — key patterns in MAND:
14. Alanine — may be ↓
15. Glutamic acid — may be ↓ (consumed for glutathione synthesis / TCA anaplerosis)
16. Glycine, serine — may be ↓ (glutathione precursors)
17. Lysine — may be ↓ (catabolic consumption)
18. Histidine — may be ↓
19. Cystathionine — may be ↑ (upregulated transsulfuration)
20. Branched-chain amino acids (leucine, isoleucine, valine)
21. Tryptophan and kynurenine pathway metabolites
22. Proline, hydroxyproline (collagen turnover)
23. GLUTATHIONE / OXIDATIVE STRESS
24. Reduced glutathione (GSH) and oxidized glutathione (GSSG) with GSH:GSSG ratio — time-sensitive sample
25. Glutathione peroxidase activity
26. 8-OHdG (8-hydroxy-2'-deoxyguanosine) — urine or blood (DNA oxidative damage)
27. Pyroglutamic acid (5-oxoproline) — on urinary organic acids (↑ when glutathione depleted)
28. Plasma cysteine
29. Plasma homocysteine (F)
30. IRON STUDIES — FULL PANEL (F)

Order ALL together to distinguish true deficiency vs. maldistribution:

- Serum ferritin — may be ↓ due to ↓ Fth1 expression, NOT necessarily true iron deficiency

- Serum iron
- TIBC (Total Iron Binding Capacity)
- Transferrin saturation
- Soluble transferrin receptor (sTfR)
- CBC with reticulocyte count
- Reticulocyte hemoglobin content (CHr/Ret-He)

Interpretation key:

- True deficiency: ↓ ferritin, ↓ serum iron, ↑ TIBC, ↓ Tsat, ↑ sTfR → iron supplementation appropriate
- MAND maldistribution: ↓ ferritin, normal/↑ serum iron, normal TIBC, normal/↑ Tsat, normal/↓ sTfR → iron supplementation may be harmful; consult metabolic/genetics
- GLUCOSE / GROWTH HORMONE (F for glucose/insulin)
- Fasting glucose and insulin
- HbA1c — low value may indicate chronic hypoglycemia
- IGF-1
- IGFBP-3
- Consider continuous glucose monitoring (CGM) if symptomatic hypoglycemia suspected

Note: Low IGF-1 alone CANNOT diagnose GH deficiency (sensitivity 68.5%, specificity 41.7% — Iwayama et al., Sci Rep 2021). Requires stimulation testing by pediatric endocrinology.

1. NUTRITIONAL COFACTORS / MICRONUTRIENTS

B vitamins and functional markers:

- Vitamin B1 (thiamine) — cofactor for PDH (the overactive enzyme in MAND)
- Vitamin B2 (riboflavin) — Complex I/II cofactor

- Vitamin B3 (niacin) — NAD+ precursor
- Vitamin B6 (pyridoxine/PLP)
- Serum B12
- Serum folate / RBC folate
- Methylmalonic acid (MMA) — functional B12 marker
- Homocysteine — functional B12/folate marker

MMA/Homocysteine interpretation:

- ↑ MMA + ↑ homocysteine = functional B12 deficiency
- Normal MMA + ↑ homocysteine = folate deficiency
- ↑ MMA + normal homocysteine = early/tissue-specific B12 deficiency

Fat-soluble vitamins:

- Vitamin D (25-OH)
- Vitamin E

Minerals:

- Zinc
- Selenium — essential for glutathione peroxidase activity
- RBC magnesium (preferred over serum)
- Copper
- Ceruloplasmin — particularly important given COX17/Complex IV connection in MAND

Other:

- Plasma CoQ10
- Free and total carnitine

CAUTION — NAC (N-Acetylcysteine):

If considering NAC for glutathione support, be aware it is a potent biofilm disruptor. May cause increased immune activation against gut bacteria → paradoxical ↑ oxidative stress. Start low, monitor GI symptoms. Consider liposomal glutathione or glycine as safer alternatives initially.

Key References:

- Meguro-Horike M, et al. BBRC. 2026;800:153288. (PDK1, COX17, mitochondrial respiration)
- Tao Y, et al. Br J Haematol. 2014;166(2):279-91. (Fth1/iron regulation)
- Du Y, et al. PLoS One. 2012;7(10):e47358. (Glucose/GH homeostasis)
- Iwayama H, et al. Sci Rep. 2021;11(1):16159. (IGF-1 diagnostic limitations)
- Bjørklund G, et al. Free Radic Biol Med. 2020;160:149-162. (Glutathione/ASD)
- Pasricha SR, et al. Lancet. 2021;397(10270):233-248. (Iron deficiency workup)
- Dinicola S, et al. Eur Rev Med Pharmacol Sci. 2014;18(19):2942-8. (NAC/biofilm)