MAND Lab Handout #4: Iron Studies — Special Considerations for MAND

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 Iron Testing for MAND — Why It's Different

What is this testing for?

Iron is essential for carrying oxygen in the blood and for making energy in the mitochondria. However, research on MBD5 (the gene affected in MAND) has shown that this gene directly controls how the body stores iron. Specifically, MBD5 helps turn on a gene called Fth1, which makes ferritin H — the protein that safely locks iron away inside cells.

When MBD5 is only working at half capacity (as in MAND), the body may not make enough ferritin H. This means iron may not be stored safely, even though it is being absorbed normally.

Why this matters — the iron paradox in MAND:

Many children with MAND have LOW ferritin levels on blood tests. This usually leads doctors to diagnose iron deficiency and prescribe iron supplements. However, in MAND, low ferritin may NOT mean the body lacks iron. Instead, it may mean:

- The body is making less ferritin protein (because MBD5 is not fully activating the ferritin gene)
- Iron is present inside cells but in a "loose" form (called labile iron) that is NOT safely stored
- This loose iron can damage cells and mitochondria by creating harmful molecules called free radicals

Giving iron supplements to a child whose problem is iron STORAGE (not iron INTAKE) could potentially make things worse by adding more loose iron to cells that cannot safely store it.

Tests that should be ordered together:

- Serum ferritin: May be low in MAND — but this may reflect reduced ferritin production, not true iron depletion.
- Serum iron: The amount of iron circulating in the blood. May be normal or even mildly elevated in MAND (unlike true iron deficiency, where it is low).
- TIBC (Total Iron Binding Capacity): Measures how much room is left on the iron-carrying protein (transferrin). In true iron deficiency, TIBC is high. In MAND, it may be normal.
- Transferrin saturation: The percentage of iron-carrying capacity that is being used. In true iron deficiency, this is low (below 20%). In MAND, it may be normal or even mildly elevated — this is a key distinguishing feature.
- Soluble transferrin receptor (sTfR): This goes up when tissues truly need more iron. In MAND, it may be normal or low (because tissues actually have iron — it is just in the wrong form).
- CBC with reticulocyte count: Checks for anemia and how well the bone marrow is making red blood cells.
- Reticulocyte hemoglobin content: Shows whether enough iron is available for making new red blood cells.

How to interpret the results — a critical distinction:

True Iron Deficiency:

- Low ferritin, low serum iron, high TIBC, low transferrin saturation, high sTfR
- Iron supplements are appropriate

Possible MAND-Related Iron Maldistribution:

- Low ferritin, BUT normal or mildly elevated serum iron, normal TIBC, normal or elevated transferrin saturation, normal or low sTfR

- Iron supplements may NOT be appropriate and could potentially be harmful
- Further evaluation and specialist consultation recommended

Important: Do not start or stop iron supplements based on this handout alone. Discuss these results with a provider who understands the MBD5-iron connection. If the pattern suggests iron maldistribution rather than true deficiency, a genetics or metabolic specialist should be consulted.

How to prepare:

- Fasting is preferred (ideally morning draw before eating)
- Iron supplements should be held for 24–48 hours before testing (ask the provider)
- Blood is drawn from a vein (standard blood draw)

References:

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- Kakhlon O, et al. "Repression of the Heavy Ferritin Chain Increases the Labile Iron Pool of Human K562 Cells." Biochemical Journal. 2001;356(Pt 2):311-6.