MTHFR

Below is the write-up we have on MTHFR. It includes general comments describing/explaining the condition; as well as replies to doctors who previously asked questions on the condition as related to themselves or their patients.

1. We can do much to help people who have been cursed with the evermore popular MTHFR deficiency diagnosis --- but, we generally need more information.

2. Who diagnosed it, on what basis was it diagnosed, and why was that doctor even looking for it? (For most doctors, it is a pseudo-scientific means to look impressive, and to separate people from their money.)

3. You may or may not understand that an MTHFR deficiency is a matter of degree, not an absolute lack of the enzyme. A person who totally lacked the enzyme, would have died in infancy.

4. Most patients (or their quacky doctors) have been reading all sorts of trash on the internet. You really should stick to the legitimate research publications, or you will be severely misled.

5. A summary on folate nutrition is written up on the NUTRI-SPEC website. The information is not as relates specifically to MTHFR deficiency, but gives you some idea of what the many physiological roles of folate are.

   You must understand that the MTHFR enzyme involves only one of many, many functions of folate. It reduces methylenetetrahydrofolate to methyltetrahydrofolate. Methyltetrahydrofolate functions to reconvert homocysteine back to the amino acid methionine. Thus, the principle danger of MTHFR deficiency is some degree of homocysteine buildup in the body --- and elevated homocysteine is one primary risk factor for cardiovascular disease.

   However --- people with MTHFR deficiency vary tremendously in their degree of deficiency. For some, it is an almost clinically insignificant condition. For some, however, there is a need for extra folate supplementation.

   Another consideration is that MTHFR is not the only mechanism by which homocysteine is reconverted to methionine. The other pathway (which is just as effective) uses betaine instead of folate. [You will note that betaine appears in significant quantities in many NUTRI-SPEC supplements.]

6. I have no idea where the notion comes from that MTHFR patients should not take folic acid or vitamin B12 supplements. First, there is no direct connection between folate status and B12 status. Second, anyone who made "recommendations not to take folic acid because it is not processed anyway" is dangerously ignorant. If you do a PubMed search on MTHFR and folate supplementation, you will find numerous studies indicating that those with MTHFR deficiency need higher than normal doses of folic acid. One such study is:

   Ozer, et al. Retrospective approach to MTHFR mutations in children. Pediatric Neurology, July 2011.

   ----- The abstract of this study ends with the statement, "…pregnant women with an MTHFR mutation may require higher than normally recommended doses of folic acid supplementation for optimum health."

7. The best way to totally evaluate folate status is by doing an Organic Acid Profile of a first morning urine void through Genova lab. The Organic Acid Profile includes formimino glutamate and methyl valerate as well as other metabolic intermediaries in folate and B12 metabolism.

8. My understanding is that mutation A1298C is not associated with pathology. Geneova lab may be correct that there is a 20% or more decreased inactivity of the MTHFR enzyme as a result of this mutation, but I expect that a difference of 20% or even 30% is far less than the difference in folate activity that occurs between people just based on dietary intake. I think the best evidence that this mutation is clinically not significant is that it is not associated with elevated homocysteine.

9. The C677T mutation is a different story. It is definitely associated with folacin metabolism problems, and particularly with elevated homocysteine. Do people with this mutation need special folacin supplementation? Probably in most cases. How much? Enough to keep both formiminoglutamate and homocysteine within normal limits.

10. What do I consider normal for homocysteine? I like to see it under 8. Anything above 12 I consider a serious problem requiring clinical intervention. NUTRI-SPEC generally covers what most patients need, but sometimes extra betaine is needed (--- betaine anhydrous, not betaine HCL). Betaine is in Diphasic AM.

11. There is no doubt that 5-MTHF will upregulate methylation in those that are in a state of hypomethylation. But the saturation point of the 5-MTHF methylation pathway is reached at something not too far above the nutrition/vitamin need for folate. In other words, 5-MTHF does not act as a

drug, “stimulating” methylation, nor does it work via the law of mass action beyond a certain saturation point.

For cancer patients, the level of 5-MTHF supplementation a well-meaning nutritionist recommends to increase methylation could conceivably accelerate the proliferation of cancer cells.

12. On the other hand, betaine is probably consistently more effective in increasing methylation for those in a hypomethylation state. Since betaine is anti-Dysaerobic, I would not be too excited about using it in large therapeutic doses for cancer patients either, but I would be more secure than I would be with folate.

13. One study you might find informative is:

Butler, et al. Prediagnostic levels of serum one-carbon metabolites and risk of hepatocellular carcinoma. The Journal Cancer Epidemiological Markers and Prevention, October 2013.

This study expands on the well-known fact that test animals deficient in choline develop hepatocellular carcinoma --- and --- the tumor DNA is hypomethylated. It is thus generally concluded that hypomethylation is an underlying mechanism for this form of cancer. --- This study went on to look at the incidence of hepatocellular carcinoma in humans and found that the incidence correlated perfectly and indirectly with both serum choline and serum pyridoxyl-5-phosphate. There was no either increased or decreased cancer incidence association with either 5-MTHF nor with betaine nor with homocysteine.

My takeaway from this is that no amount of supplementation with betaine or 5-MTHF in cancer patients is going to either prevent or cure cancer --- even if it improves the methylation state and decreases homocysteine.