MTHFR

GENETIC VARIATION & FERTILITY

FERTILITY MOM

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Methylation

YOUR BODY'S KEY TO OPTIMAL HEALTH & FERTILITY

One of the most important processes that needs to happen inside the body is something called methylation. Methylation controls our genetic expression; it can turn genes on or off and every single gene in every cell is regulated by methylation.

Methylation is the process of adding a methyl group made of 1 carbon atom and 3 hydrogen atoms to something in your body like a protein, enzyme, gene, hormone, etc.



Hundreds of reactions in the body need methylation to occur properly. Not only does methylation turn genes on or off, but this process is also involved in repairing and building DNA/RNA, detoxifying chemicals and excess hormones, regulating the stress response, reducing histamine, and repairing cell membranes.

Without proper methylation, egg and sperm health can be of poor quality making pregnancy achievement impossible. A deficient methylation cycle can be the cause of many pregnancy and fertility issues including recurrent miscarriages, neural tube defects, and congenital heart defects.

There are many genes involved in the entire methylation cycle but one of the most important is the MTHFR gene. When this gene is deficient then the entire methylation cycle will suffer.

MTHFR GENE

The job of the MTHFR gene is to methylate folate to create methylfolate. This methylfolate, or active folate, then becomes a critical part of the methylation cycle. Without enough methylfolate our entire methylation cycle cannot function properly and all 200+ functions throughout the body suffer, including our fertility.



As discussed in module 2, the above is a simple representation of the methylation cycle. The MTHFR gene, along with vitamin B2, is responsible for taking 5, 10-methylene THF (tetrahydrofolate) and making methylfolate (5-MTHF). That 5-MTHF is then taken by vitamin B12 into over to SAM, who distributes the methyl groups throughout the body for all the processes necessary.

When the MTHFR gene has a variation then its ability to create methylfolate is decreased, which results in a deficient methylation cycle. This can cause issues with detoxification, energy production, egg and sperm health, cell repair, inflammation, stress response, antioxidant production, genetic expression, and more.

Approximately 50-60% of us have an MTHFR genetic variation of some sort impacting our ability to methylate, and this issue is generally not found until a woman has been having problems getting or staying pregnant.

There are up to 30 different genetic variations for the MTHFR gene, but the 2 most commonly studied variations are the C677T and A1298C. If you've had MTHFR testing done then the results show you have one or both of these variations.

- C677T variation significantly reduces methylfolate level
 - 1 copy of C677T = heterozygous C677T = 35% reduction in MTHFR activity
 - 2 copies = homozygous C677T = 70% reduction in MTHFR activity
- MTHFR A1298C mildly reduces methylfolate level
 - 1 copy = heterozygous A1298C = no significant issue
 - 2 copies = homozygous A1298C= 35% reduction in MTHFR activity
- One compound of each C677T & A1298C = 50-60% MTHFR activity

Any genetic variation of the MTHFR gene is important to address when trying to get and stay pregnant. One of my biggest frustrations is that many women are simply told, "it's not a big deal, just take more folic acid" because this is not an adequate approach.

First off, folic acid is a methylation cycle **blocker**. Folic acid is the synthetic version of folate and is not useful inside the body unless the body processes it into its active form. Unfortunately, this process is done by DHFR, a slow enzyme that can only handle 200-300mg of folic acid PER DAY. This creates a problem because many women are told to take up to 5,000mg of folic acid when they are found to have an MTHFR variation, which means that the vast majority of that folic acid is roaming around the body as unmetabolized folic acid (UMFA). UMFA has been known to cause immunity issues, NK cell disruption, as well as even increasing cancer risk in some populations.

One of the biggest issues with folic acid is that it blocks the uptake of real folate. Folic acid resembles folate and occupies the folate receptor, therefore blocking real folate from getting into the cell. This decreases the body's ability to methylate even more. For this reason, it is extremely important that you avoid enriched foods containing folic acid like breads, cereals, pastas, flours, cornmeal, etc.

If you have not had any genetic testing but worry you may have an MTHFR variant, I encourage you to speak with your doctor, but there are also physical signs and symptoms that you can assess to see whether your methylation cycle is deficient.

MTHFR GENETIC VARIATION ASSESSMENT

It is possible to assess whether you're at risk for an MTHFR gene variation outside of getting genetic testing. Check all that apply:

I suffer from headaches	
I struggle with depression	
I have a family history of miscarriage	
I have a personal history of miscarriage	
I have a family history of depression where antidepressants did not work	
I have cold hands or feet	
I get menstrual cramping and clots during my period	
My folate and/or B12 levels are elevated	
My homocysteine level is high (Over 12mmol/L)	
I rarely eat green, leafy vegetables	
I feel better when I eat green leafy vegetables	
I am irritable and have a quick temper	
I take folic acid supplements and/or eat enriched foods	

If you checked 5+ boxes it is likely you have an MTHFR gene and/or methylation cycle that is working less than optimally. The good news is: <u>you can change this using our</u> <u>epigenetic factors!</u>

ADDITIONAL TESTING

Homocysteine

After SAM passes off its methyl groups around the body it changes into homocysteine. Homocysteine can then either be recycled back into the methylation cycle or it can be used to make glutathione, the body's master antioxidant. Many doctors will test homocysteine levels believing this gives an accurate picture of how well the methylation cycle is working but this is not quite the full picture.

Most lab value ranges and doctors will consider a homocysteine level 'normal' at anything below 15 μ mol/L (micromoles per liter) and 'high' at levels above this. However, experts in methylation consider anything above 7 μ mol/L to be high. I

Serum Folate

This lab is a bit confusing because it measures both synthetic folic acid *and* natural folates. This lab value really only means something if you're not taking any folic acid in any form whatsoever. If you have a high level (without taking folic acid or eating any folic acid enriched foods), then you might be having problems with your gut, folate receptor antibodies, low vitamin B12, or a blocked methylation cycle. If you have low readings, then you need to increase your intake of natural food folates along with a supplement (methyltetrahydrofolate or folinic acid).

Vitamin B12

Ideally, we'd like to see B12 more than 500, but if it's on the high end of normal and being unsupplemented then it's possibly not being absorbed or used. If there is not enough B12 then there is little to no methyl usage. This can cause a reaction to taking methylated supplemented like rash (see supplement book for more). Vegetarians and vegans must always supplement with B12, but some additional signs you may be B12 deficient are sleep problems (waking throughout the night), constipated, tingling, numbness, lack of ability to concentrate, bad reaction to taking methylfolate.

*Hypothyroidism can slow your ability to activate B2, which is an important cofactor in the methylation cycle. Have your thyroid level evaluated including a full thyroid panel: TSH, Free T3, Free T4, Reverse T3, TPO antibodies, Tg antibodies

MANAGING AN MTHFR GENE VARIATION AND OPTIMIZING THE METHYLATION CYCLE

Successful support of the methylation cycle includes:

- Eating in the Fertile Food Plan
- Eliminating all folic acid intake, including from enriched foods
- Eating green leafy greens daily (2-4 cups per day)
- Supplementing with methylated vitamins, if tolerated, or unmethylated folinic acid (see supplement book)
 - Dosing for homozygous C677T can be a total of ~3500mg of folate; heterozygous ~2000mg of folate; A1298C/C677T mixed ~2500-3000mg
 - IN ADDITION to eating daily green leafy vegetables to increase the food folate intake
 - Doses of up to 7.5grams of methylfolate can be taken (7500mg) but this must be slow and you should be feeling better every time you increase a dose. Generally doses in the 2000-3500mg range plus eating food folate is adequate.
- If vegan or vegetarian, then supplementing with B12 *and* choline is a <u>must</u> (see supplement book)
- Supplement with Riboflavin (B2), especially if suffering from migraines
 - Riboflavin-5-phosphate is the active form, dose of 20mg to start and is usually adequate
 - If you have severe migraines, doses of up to 400mg may be necessary. Again, start low and go slow.
- Assess whether you have a dairy intolerance through an elimination protocol dairy can contribute to producing folate receptor antibodies
- Support the liver -- 85% of all methylation takes place here!
 - Decrease intake of alcohol
 - Avoid chemicals and toxins (Toxin Elimination Plan)
 - Support detoxification with daily detox drink, NAC, and food plan