MTHFR

MTHFR (Methylenetetrahydrofolate reductase) is a common genetic variant that causes a key enzyme in the body to function at a lower than normal rate. This can lead to a variety of medical problems when people with MTHFR are exposed to more toxins than their bodies can handle. There are more than 50 known MTHFR variants, but the two prime variants are 677 and 1298; the numbers refer to their location on the gene. The routine lab test for MTHFR variant only reports on 677T and 1298C since these are the most studied.

The 677T variant is most commonly associated with early heart disease and stroke, and the 1298C variant with a variety of chronic illnesses. Either anomaly can cause a wide variety of health problems. The MTHFR anomaly is heterozygous or homozygous. If you're heterozygous, that means you have one affected gene and one normal gene. The MTHFR enzyme will run at about 55 percent to 70 percent efficiency compared to a normal MTHFR enzyme.

If you are homozygous, then enzyme efficiency drops down from 7 percent to 10 percent of normal, which, of course, makes a huge difference. The worst combination is 677T/1298C in which you're heterozygous to both anomalies. Many chronic illnesses link to this anomaly. Autistic children have an MTHFR anomaly at a rate of 98 percent. Fibromyalgia, irritable bowel syndrome, and migraines, are all conditions associated with MTHFR anomaly. We have also rarely seen patients homozygous with 677T and heterozygous 1298C, but this is very rare.

MTHFR can make you susceptible to illness because the pathway is the primary source of glutathione production in the body. Glutathione is the body's primary antioxidant and detoxifier. People with MTHFR anomalies usually have low glutathione, which makes them more susceptible to stress and less tolerant to toxins. As we age, MTHFR problems worsen due to the

accumulation of toxins and the cumulative effect of oxidative stress.

Treatment

Fortunately, we can now easily test for MTHFR and augment the essential nutrients the MTHFR enzyme makes, which is methyl B12, the active form of B12 and glutathione, the end product of the pathway. There are prescription medical foods that help; Deplin, Metanx, Nees, and Cerefolin NAC are a few of the compounds available. Methyl B12 is available as shots, nasal sprays, and sublingual drops. The shots are by far the most effective method. There are other supplements like SAMe, TMG, and Betaine that can augment the methylation pathway. However, some of these compounds, especially SAMe, may actually make things worse in some people. Biopterin, commonly referred to as BH4, is another compound that's sometimes very helpful, especially in diabetes and chronic depression.

The choice of nutrients will vary from patient to patient. Having adequate levels of B vitamins is important, since lack of B vitamins, especially vitamin B6, may cause problems in the pathway.

The choice of treatments is somewhat dependent on the nature of the anomaly. I have found, in the 1298 anomaly, methyl B12 works very well and in the 677 anomaly, L-methyl folate (Deplin, Metanx, some supplements) is most helpful. Although, I often use multiple compounds to augment the pathway at several points.

Once we confirm MTHFR variation, then it's possible to take a number of steps to minimize health problems due to MTHFR. The treatment of MTHFR-related problems is primarily nutritional. There are a number of prescription medications, classified as medical foods, that help with this disorder. The two that I use the most are Metanx and Deplin. These links take you to

the pharmaceutical websites, which do not discuss the full range of conditions for which these medications are useful.

Treatment of patients with MTHFR-related issues range from simple to complex, depending on a variety of factors, including lifestyle, diet, and overall accumulated toxicity. There are two primary issues: The first is augmenting the pathway to produce adequate glutathione, and the second is dealing with the accumulated toxic load. This second issue makes treating MTHFR-related problems tricky. When glutathione levels go up, the body will start excreting these accumulated toxins, mostly through the liver, which excretes the toxins into bile. The bile then moves into the intestinal tract, and the toxins release and reabsorb, which can cause a whole variety of nasty side effects. You can minimize these side effects by using compounds to bind up bile in the GI tract, such as toxin-free, activated charcoal; modified fruit pectin; and cholestyramine, a drug used to bind bile. Many of these problems are avoidable by starting the treatment of the methylation pathway slowly, that is, to start with smaller than maintenance doses and ramp up the pathway slowly.

Do You Have MTHFR or Methyl Issues?

If you haven't had tests and have chronic disease(s), the first place to start is with genetic testing. Tests for the common MTHFR anomalies cost around $150 to $350 at most laboratories. Your insurance may cover the test, but in most cases, it doesn't. We have found a better solution for most patients, as long as time is not an issue. We use 23 and me, a genetic testing site, to obtain the raw genetic data. We then load that data into a third-party application to get a much more complete genetic picture of methylation and detoxification. Not only is the information much more complete (more than 50 snips versus two), it's also much less expensive, just $99 for the genetic profile and another $20

for the third-party application.

Treatment Tip: An adverse reaction to treatment often means you're on the right track but need to change the dose or rate of treatment. The same nutrient given at lower dose may help. You may also need more B vitamins, especially vitamin B6.

I've put together a couple of mind maps that will help you visualize the condition. There's also a link to information put together by Dr. Neil Rawlins, including a number of his lectures on MTHFR. My mind maps closely follow his lecture notes. I wish to thank Dr. Rawlins for all the work he does in this area. While MTHFR was something I knew about, his lectures made me realize that MTHFR was a primary cause of many of my patient's health problems.

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My key recommendations to patients with chronic medical disorders are:

- Get evaluated for MTHFR. It's a simple blood test costing about $160.
- Better yet get a much more complete genetic evaluation for just $99.

- Consult with a physician who knows how to treat MTHFR-related problems.

The first link will take you to Neil Rawlins's site, where you can download his series of lectures on MTHFR. A mind map

is a way to present complex material in a graphic fashion. These maps are on Mindmeister.com

Dr. Neil Rawlins' Lectures and Notes on MTHFR
MTHFR related medical conditions
MTHFR Treatment

http://www.mindmeister.com/12721370ichard van Konynenburg Lectures. This is a long highly technical lecture on ME (myalgic encephalopathy) or chronic fatigue syndrome. He demonstrates how the biochemistry of methylation plays a role in chronic disease. This lecture is simply fabulous.

From the site:

Rich Van Konynenburg's formal education was in engineering and the applied physical sciences. He received a PhD degree from the University of California-Davis in 1974. He served as an officer in the U.S. Army Corps of Engineers for two years and worked for the University of California at Lawrence Livermore National Laboratory for 30 years, doing research and development in nuclear materials and technology.

He has studied chronic fatigue syndrome (CFS) for the past 15 years. In 2007, he proposed a hypothesis for the pathogenesis and pathophysiology of CFS, called the "Glutathione Depletion–Methylation Cycle Block" hypothesis.

Dr. Van Konynenburg's hypothesis includes both mercury toxicity and electromagnetic sensitivity as both causes and consequences of CFS.

Based on his hypothesis, he has been encouraging the application of methylation cycle treatment (originally developed to treat autism), to the treatment of CFS. This type of treatment was found in a clinical study to provide significant benefit to about two-thirds of the CFS patients who participated, and its use is growing in the CFS community

internationally.