# The MTHFR Connection

By James P. Johnston, D.O. (July 14, 2023)

The COVID pandemic taught me something new about the human body, and its application might be much more widespread and relevant than simply reversing the symptoms of Long Haul COVID-19! It has me going back to the drawing board, so to speak, wondering if many chronic problems could be remedied by reevaluating symptoms in the light of this discovery.

**My Growth in Understanding**

A drug came to market about 15 years ago called Metanx (which was 6 mg of L-methyl folate, or methylated folate, plus some other B vitamins thrown in). Actually, Metanx wasn't categorized as a drug, but the FDA labeled it "medical food." There wasn't an over-the-counter equivalent, but since it was a methylated form of folic acid, and since folic acid was an over-the-counter supplement, it was labeled "medical food", and therefore, not covered by most insurances very well.

I prescribed it a lot for multiple problems because it was a natural remedy with far less side effects than the more artificial competitors.

Branded L-methyl folate earned several indications from the FDA:

**Metanx** got an indication for 1. peripheral neuropathy; 2. normalizing folate levels in patients with a homozygous MTHFR mutation. and 3. hyperhomocysteinemia (which was a factor in premature heart disease.) It's dose was 3 mg twice daily.

In the form of **Deplin**, L-methyl folate earned the indication for depression. The L-methyl folate dose was higher in Deplin at 15 mg.

In the form of **Cerefolin NAC**, it earned the indication for dementia, with a different combination of vitamins added in.

Rather than treating symptoms, I was getting to the root of the problem. And there were so few side effects! It's the only anti-depressant that didn't cause bipolar depressed patients to go manic (like SSRIs do), and which don't increase suicide risk in teens. It's sad that the meds most commonly used to treat depression in teens actually increased the risk of suicide! **"First, do no harm"** is a common physician ethics mantra, and it's very relevant. I far prefer Deplin to SSRIs in depressed teens unresponsive to counseling, though it was cost prohibitive for most families.

Even though L-methyl folate had so few side effects, the patients who needed it most were often the patients who complained that it felt too strong! I had to explain to them: imagine the cells of your body are starving for L-methyl folate like the desert sand starves for rain. When a rainstorm comes to desert sands, what happens? The hot sands suck up the water as quickly as it can, but often the deluge causes dangerous rises in water that can cause erosion and dangerous water streams due to lack of inability to absorb it quickly enough (watch the dangerous flood of a rare rain torrent in a desert).

That's what happens to the bodies of many people who have the MTHFR mutation, especially if they're homozygous. If you don't have that mutation, it causes no more side effects than a B-complex multivitamin. If you have side effects on it, it's because you need it so badly. Therefore, my remedy was to titrate it slower than even recommended by the drug company.

Most doctors didn't prescribe these meds much because insurances didn't cover it due to its "medical food" categorization by the FDA.

**The Symptoms**

An MTHFR mutation can be responsible for:

*Infertility, stillbirths, & miscarriages
*Chronic headaches and migraines
*Childhood behavior disorders
*Depression
*Anxiety
*Bipolar disorder
*Psychotic disorders like schizophrenia
*Allergies and sensitivities
*Gastrointestinal health and difficulty detoxifying chemicals like thimerosol and endocrine disruptors like measurable pesticides and herbicides in our food
*Insomnia
*Hormonal conditions
*Cardiovascular diseases like stroke and heart attack
*Poor healing of wounds and slow recovery of infections
*Dementia
*Colon cancer
*Leukemia
*Autoimmune diseases, like Hashimotos or lupus
*Fibromyalgia
*Neural tube defects in preborn children (like spina bifida and anencephaly)

It has been thought that heterozygous patients do not have these symptoms. That one good gene is all we need to metabolize enough folic acid from our diet. Looking back at the initial studies which got Metanx/Deplin/Cerefolin NAC their indications, I came to a different conclusion.

**The Mystery**

This was something I did not realize until years later, but the indications for L-methyl folate were obtained from studies in the general population. They weren't targeted to MTHFR mutated patients. Those homozygous for the MTHFR mutation comprise about 15-20% of the population. If all that was special about these prescription-only supplement pill was the methylated folate, why didn't the drug company target homozygous patients who were the ones expected to have the greatest benefit?

It's because, either the drug manufacturers believed that the heterozygous patients could still benefit from it, or they thought the B vitamins may be beneficial against placebo for most Americans regardless of MTHFR status. Most researchers believe that heterozygous patients (that is, patients with one good gene from one parent and one mutated gene from another parent), do not have symptoms. If I order an MTHFR DNA analysis from Labcorp, and the patient is heterozygous, Labcorp includes a lengthy clause explaining that heterozygous patients aren't symptomatic.

I no longer believe that this is the case. <u>I am convinced that heterozygous patients often do have symptoms.</u>

**The Imposters**

A few years after Metanx/Deplin/Cerefolin NAC came to market, China flooded the market with a cheap generic, violating the drug manufacturer's legal patient. I guess the Chinese drug company suspected the branded drug manufacturer wouldn't sue to have their patent upheld due to so few doctors prescribing it. Regardless, the generic was cheaper, and so I switched almost all of my patients over to the generic.

Without fail, 90% of my patients on one of these three medicines contacted me within a couple months wanting to go back on the branded med. The generic simply did not work as well. The drug manufacturer finally sued and got its patent enforced by the FDA, and all my patients went back on the name branded L-methyl folate. However, now, its patent has ended and there are a lot of generics as well as over-the-counter alternatives on the market. But because it's "medical food" categorization and my experience with generic alternatives to L-methyl folate, I don't trust the generic and over-the-counter alternatives. Too many patients are not getting symptom relief on the generics and over-the-counter alternatives as they did on the name brand drug.

**The Science**

There are two MTHFR genes that are necessary to metabolize folic acid from our diet. Folic acid is a precursor to hormones, neurotransmitters, and many other important functions in our body. If a patient is homozygous for one of these two genes (that is, got bad genes from both parents), they were often mentally unhealthy and sickly as children.

(Feel free to skip the rest of this section if the science is uninteresting to you.) The two genes and their prevalence are as follows:

- **C677T:** About 30 to 40% of Americans may have at least one mutation at gene position C677T. Homozygous patients are more rare. Roughly 25 percent of people of Hispanic descent and 10 to 15 percent of Caucasian descent are homozygous for this variant.
- **A1298C:** An A1298C mutation is found in 7 to 14% in North Americans, with the homozygous variant being even more rare.

What does the MTHFR gene do? The MTHFR gene creates methylenetetrahydrofolate reductase (which is where we get the acronym MTHFR). This plays a central role in folate and homocysteine metabolism by catalyzing the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, the primary circulatory form of folate which is utilized in homocysteine remethylation to methionine. (Feel free to forget all that.)

Needless to say, it is VERY important for many bodily functions at the cellular level.

**You Can't Change Your Genes...**

...But you can mitigate their affect on your health and lifespan.

Genetic deformities suck. There are fatal ones, like anencephaly, significant ones, like congenital heart disease and Downs Syndrome, and there are more mild genetic deformities like

dispositions to skin cancer, diabetes, and hypercholesterolemia, and tooth problems requiring braces.

With the milder, less damaging mutations, it is easier to treat the symptoms and not take into account the root cause. Like wrinkles and graying hair, at certain ages and at certain toxic load levels we tend to break down and the genetic aberrancies inherited from our parents begin to manifest. We all tend to get our parent's and grandparent's diseases.

You can't change your genes, which are in every cell of your body, but what if you can negate all the negative consequences of that dysfunctional gene? With L-methylated folate taken orally, we can bypass this genetic mutation and resolve many medical problems before they start, at the foundational cellular level.

**The Controversy**

When the research about MTHFR started coming out, I began to prescribe Metanx to every patient with a family history of cardiovascular disease and dementia. With the drug manufacturers samples and coupons, and me stressing to the patient the importance of this prescription supplement to get to the root cause of so many life-threatening diseases, I had a good success rate in getting patients to stay on it.

But many cardiologists weren't getting on board. It was thought that if there was a genetic problem that resulted in difficulty methylating folic acid to make it bioavailable, all they had to do was prescribe folic acid. So in homozygous patients, many cardiologists prescribed ten times the recommended dose of folic acid, as if that would someone overcome the genetic difficulty the body had in metabolizing it.

Since it was labeled as "medical food" by the FDA, many pharmacies took the liberty of substituting a script for Metanx/Deplin/Cerefolin NAC with non-methylated folic acid alternatives, and it took a class action lawsuit for pharmacies to stop it.

If an MTHFR deficiency is unable to methylate folic acid and convert it into a bioavailable form, is that unmethylated folic acid bad for you? Yes, many researchers are beginning to believe so. At best, it is not helpful.

Most researchers and physicians and laboratories are convinced that heterozygous patients did not develop symptoms related to the genetic mutation. However, I am convinced, under under stress or if they have a high "toxic load", even a heterozygous MTHFR mutation is significant. This is what I learned during the COVID pandemic.

**Vaccine Injury and Long Haul COVID**

During the COVID-19 pandemic, I treated thousands of patients all over the country with acute COVID-19, Long Haul COVID, and COVID-vaccine injuries. I learned everything I could about the pathogen and the vaccines, and followed the recommendations of the Front Line Critical

Care COVID-19 Alliance, prescribing Ivermectin and/or Hydroxychloroquine, and many evidenced-based supplements.

But the more I learned about the neurotoxicity of the M-spike protein created by the vaccine and the pathogen, the more I suspected there was more to this story than meets the eye. The more I learned about the hormonal problems and infertility and miscarriages and cardiovascular deaths associated with this pathogen and the COVID-vaccines, the more I suspected the MTHFR genes may be making all the difference.

**My First Time**

The first time I prescribed Metanx for a patient suffering from COVID, it was an elderly patient who had suffered for 10 months after her acute COVID infection. Initially, she had fever and two weeks of fever, skin pain, headaches, chest pain, numbness and tingling in her fingers, brain fog, stomach pain and bloating. When her fever and coughing ended, her suffering did not.

When I first met her, she'd been to a cardiologist for persistent palpitations and chest pain. She passed her stress test and put her on a beta blocker to lessen her palpitations, with minimal benefit. She'd been to a gastroenterologist for her chronic bloating, dyspepsia, and weight loss from lack of appetite. He did an EGD (a scope to look at the stomach), and prescribe anti-acids. She had improved little. She also went to a neurologist for her headaches, finger numbness, lost of taste and smell, and "brain fog" and was put on neuroleptics with no benefit. Ten months of suffering, tens of thousands of dollars spent on three specialists, two major procedures, and now she was depressed and considering disability and retirement.

Desperate, she ordered a one-time consult from me through my website. Of course, I prescribed the FLCCC medications and supplements, but for the first time, I tried Metanx. After all, it had an indication for peripheral neuropathy, and that was one of her main symptoms. So many of her symptoms, it could be argued, could be neurologically mediated. The palpitations could be from the M-spike protein's damage to the nerves managing heart conduction. The GI bloating could be from the M-spike protein's damage to the vagus nerve. The headaches and numbness and brain fog could have been because of the neurotoxic effect of the M-spike protein.

Surprisingly, the patient contacted me in two weeks after starting her medications, claiming to be 95% better!

**Ten months of suffering and she was 95% better in two weeks? Was it really true?**

She said, **"You have given me my life back!"**

**The Strange Dichotomy**

My brother got a COVID vaccine and has been handicapped from it ever since, with crippling difficulty-to-treat rheumatoid arthritis.

My wife's Aunt died in her sleep after her COVID vaccine.

A pastor and dear friend of mine died from his COVID infection.

Yet most people endure COVID and the vaccine with relatively few symptoms.

Why do some patients get over COVID so easily? *Half* of the people who contracted COVID and became immune to it had no symptoms at all!

Why do some patients tolerated the COVID vaccine with so little symptoms or side effects, and yet so many others have died or been disabled from it?

**I think the MTHFR genes are a major factor.**

I contacted the FLCCC asking them to put Metanx on their first line recommendation list, but not much had been written on it. One article did show a connection, concluding, "There is a clear trend toward the worldwide prevalence of *MTHFR* 677T and COVID−19 incidence and mortality." The FLCCC began to publish data on it.

Of course, the difficulty methylating folic acid is not the only factor. It's definitely multi-factorial. It is also related to your toxic load.

What do I mean by "toxic load"?

I like this metaphor. Imagine a tsunami sweeping over a beach town and wiping out most of the buildings. The small brick and lumber business on the edge of town may have been sufficient for the usual growth of the town, but after the tsunami, it's simply not efficient enough to handle the higher demand for building materials, and the town remains unliveable for much longer. In the same way, your one good MTHFR gene might be sufficient to detoxify small loads and handle minor traumas and stresses, but if you have a bad case of COVID, or a high toxic load, just like the small brick and lumber company isn't enough for the higher demand, so your poorly functioning MTHFR system cannot repair all the damage efficiently.

L-methyl folate is dropping a load of bricks and lumber in the center of town for a much speedy repair!

Since treating thousands of patient with COVID-19 and Long Haul COVID, and hundreds of patients suffering from vaccine injury, I have discovered that the symptoms in patients suffering from these problems are very similar in most cases. It's certainly in part due to the neurotoxicity of the M-spike protein, which the mRNA vaccine and the COVID-19 pathogen **both** create. But it is also likely due in part to the handicapped MTHFR system that cannot detoxify as well. The preservatives in the COVID-19 vaccines, and indeed every vaccine, are dangerous at higher levels. Fortunately, a fully functionally MTHFR system can detoxify most things like thimerosal or aluminum in vaccines, but a dysfunctional MTHFR system cannot do it as well.

It has already been proven that an MTHFR mutation increases the risk of vaccine adverse events. That is especially true with a vaccine like the COVID-19 vaccines, which all create the very

neurotoxic M-spike proteins. Folic acid is a precursor to neurotransmitters like serotonin, and if your system cannot methylate it and make it bioavailable, you're not going to be able to repair the neurologic damage very well.

Our body is flooded with many microscopic chemicals that we are supposed to detoxify, like mercury, aluminum, artificial preservatives and sweeteners, and endocrine disruptors associated with pesticides, herbicides, and other chemicals associated with eating out of plastic containers. If you have an MTHFR mutation, you cannot detoxify these impurities as well, and thus, it is important to eat organic foods. Otherwise, those levels will rise higher and there will be more health threats associated with them.

One researcher estimated: "If you have one MTHFR C677T mutation, your ability to detoxify mercury is decreased by 50%. If you have two MTHFR gene mutations at C677T, your ability to detoxify the mercury is decreased by a whopping 90%."

**Bottom Line**

To summarize, if you had neurological side effects when you contracted COVID-19, symptoms like skin pain, hair loss, paresthesias, loss of taste or smell, blurry vision, depression, palpitations or gastric bloating, especially if these symptoms lasted longer than 2 weeks, I would recommend at least a three month course of Metanx to help replenish your bioavailable folic acid levels.

If you were sickly as a child, or struggled emotionally in times of stress or crisis, such as during life transitions like puberty or menopause, moving or change of jobs, and had a difficult time getting over infections or struggled with chronic disease in your life, I might recommend Metanx life-long. You could be homozygous for the MTHFR mutation. If you're still struggling with depression, anxiety, emotional fragility, or difficulty tolerating stress, I would recommend a trial of Deplin. (I'm convinced most depressed patients could come off their SSRIs with a trial of Deplin, but this should be carefully managed by a physician.)

If you had "brain fog" more than one week with COVID, or have a family history of Alzheimers dementia, I would recommend Cerefolin NAC.

I would not recommend the generics in such cases, but would recommend the prescription. At your local pharmacy, these meds run $180 a month, but I call them into a specialty pharmacy which charges 1/3 as much. Click my website below and order a "Miscellaneous Consult" if you would like to try this, or if you would like to get tested for an MTHFR mutation. It's a non-fasting blood test, so make your appointment in the morning.

If you have an MTHFR mutation or suspect that you do, in addition to taking a prescription for name brand L-methyl folate, also do these things:
*Eat organic,
*Avoid fish high in mercury, and
*Filter your water well.

*Take these supplements from a trustworthy American-made brand: Glutathione, NAC, alpha lipoic acid, milk thistle, and selenium. You can purchase them on my fullscript account HERE. I have a 25% discount for patients who sign up for my fullscript account.

God bless you,
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