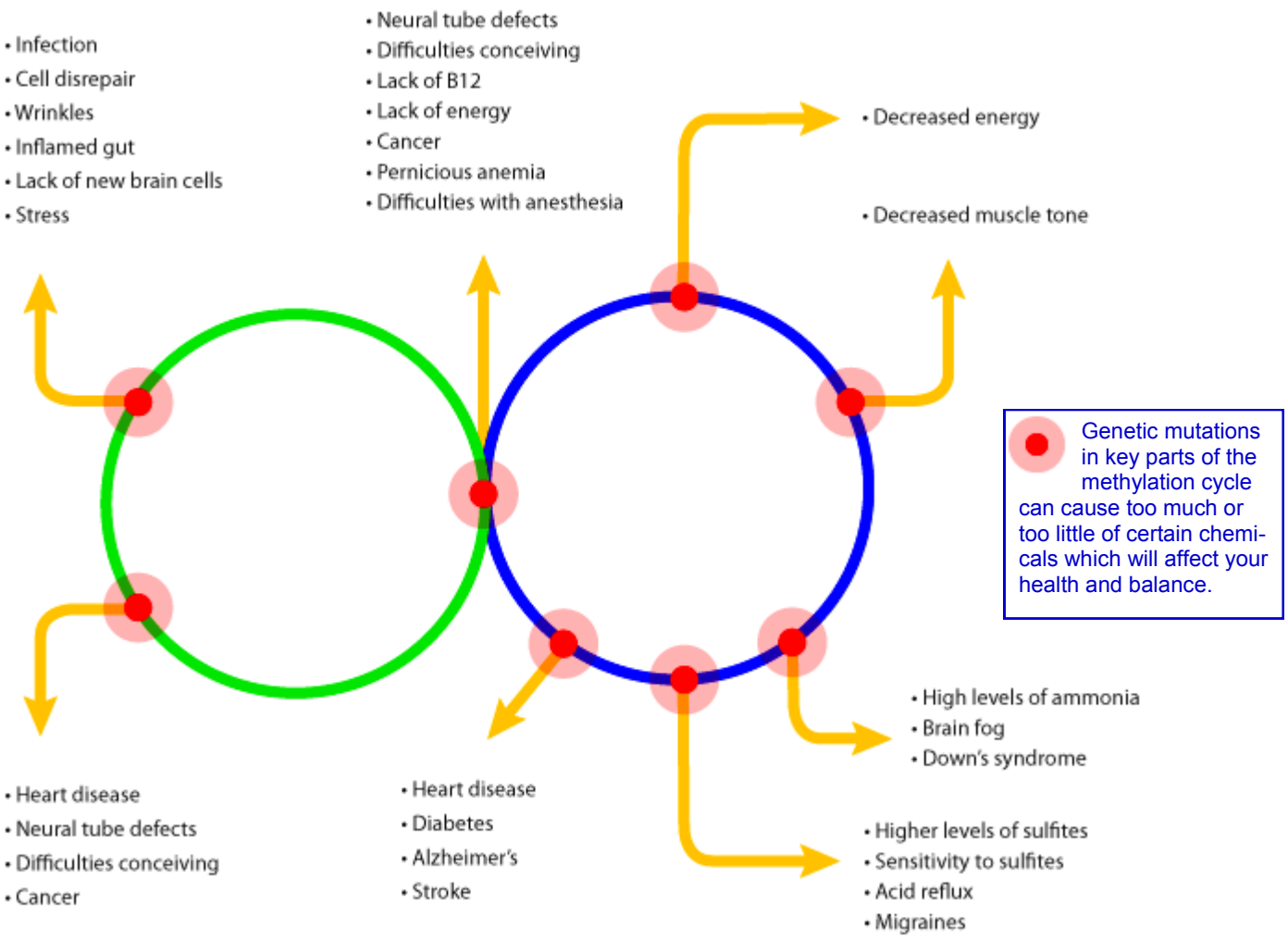
Methylation

The methylation cycle is a biochemical pathway that manages or contributes to a wide range of crucial bodily functions. Methylation is not just one specific reaction, there are hundreds of methylation reactions in the body. Methylation is simply the adding or removal of the methyl group to a compound or other element. The methylation cycle is the backbone of how we are able to function. The effectiveness of the methylation cycle determines how well our body deals with detoxification, immune function, DNA maintenance, energy production, mood balance and controls inflammation.

All these processes help the body respond to environmental stressors, to detoxify, and to adapt and rebuild. That's why lowered methylation function may contribute to many, major chronic conditions, as listed below.

Proper functioning of the methylation cycle helps to reduce the risk of:



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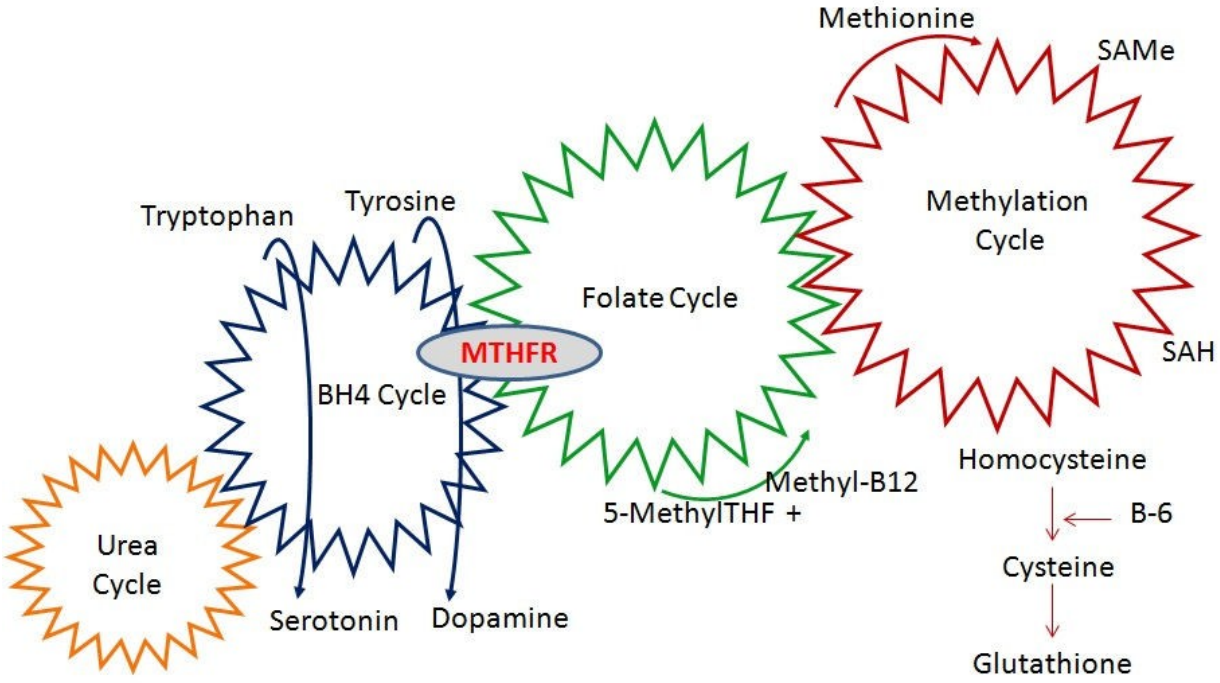
Taking the guesswork out of diagnosis

In general, when some compounds receive a methyl group, this "starts" a reaction (such as turning a gene on or activating an enzyme). When the methyl group is "lost" or removed, the reaction stops (or a gene is turned off or the enzyme is deactivated). Methylation is involved in almost every bodily biochemical reaction, and occurs billions of times every second in our cells. That's why figuring out where the methylation cycle can be improved will contribute to improvement of health, and reduce symptoms.

The biochemistry involved is complicated, but suffice it to say, a defect at any one point in these interlocking metabolic cycles will inevitably affect the remaining pathways, and your overall health will then suffer. Methylation abnormalities may explain why one person can be sick from environmental toxins while another is just fine, why one child is autistic while their fraternal twin brother is not. While a persons DNA cannot be changed, if we know where your weak links occur, we can create "nutritional by-passes" - we can supplement alternative pathways or restrict dietary molecules that you cannot process effectively. Below is a simple diagram of the biochemical pathways that are intermeshed and how a problem in the methylation cycle or other cycles, will affect how well your individual biochemistry works, ultimately determining how you feel, or what you may be susceptible to.



According to the Pfeiffer Institute, 45% of individuals are under-methylators, 15% are over-methylators, which means that 40% are neither under or over-methylators.

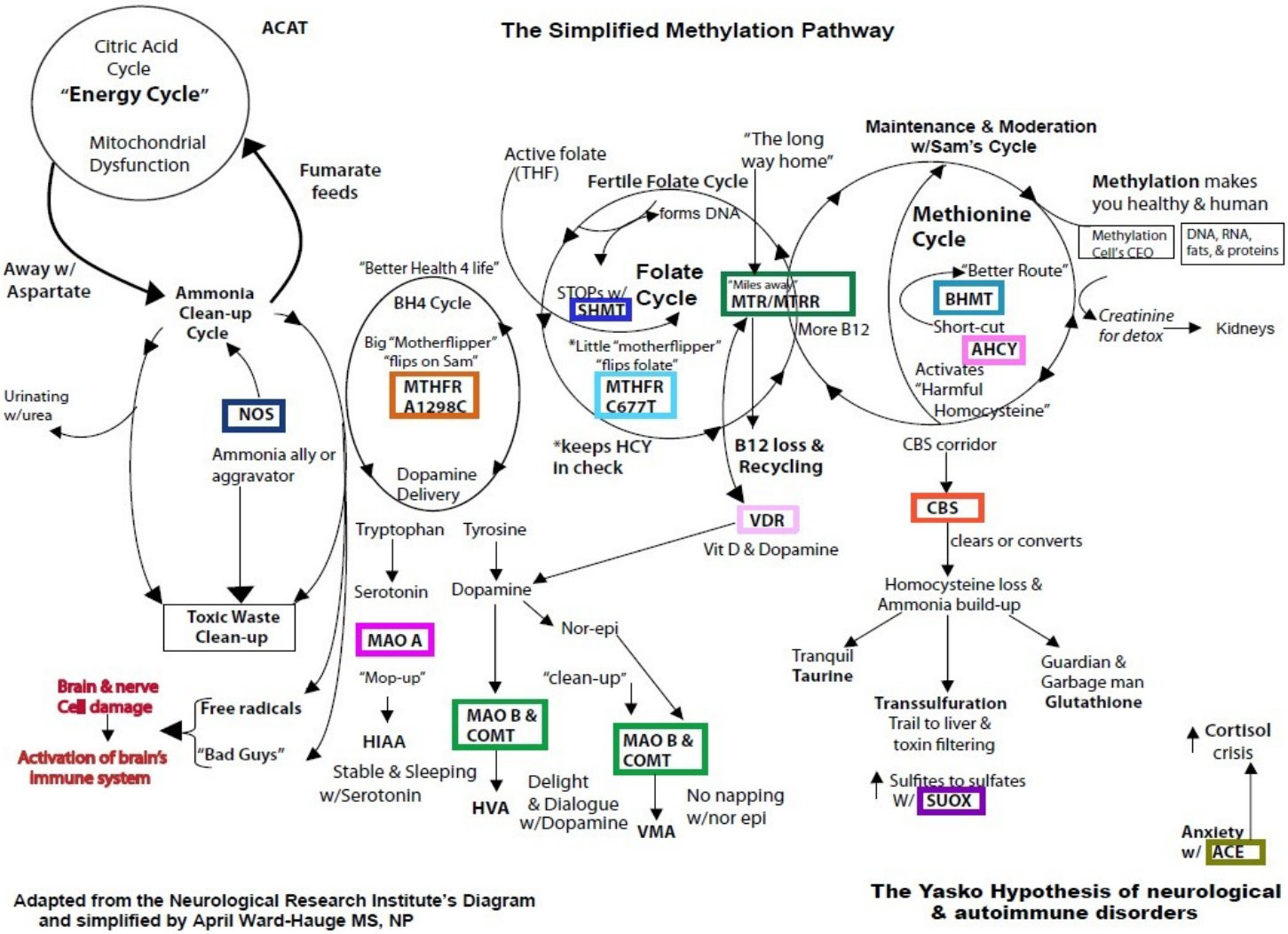
Consequences of genetic weaknesses (mutations) or nutritional deficiencies in the methylation pathway are increased risk factors leading to a number of serious health conditions (see below). This does not mean that every individual will have one of the health conditions listed below. Most health conditions in society today are multifactorial, there is an underlying genetically determined risk that requires a significant infectious or environmental "trigger" to initiate the process. Appropriate supplementation with vitamins and nutrients may be effective in by-passing these mutations to allow for restored function of the methylation pathway.

Table of some typical clinical symptoms of under or over methylation.

Clinical Symptom	Under-methylation	Over-methylation
High academic achievement	+	
Competitive	+	
Addictiveness	+	
Eating disorder	+	
Obsessive Compulsive	+	
Perfectionism	+	
Inner tension	+	
Ritualism	+	
Ruminate	+	
Psychosis	Catatonic	Active
Hirsute	N	Y
Pain threshold	Low	High
Responds to SSRI drugs	Yes	No
Responds to Benzodiazepines	No	Yes
Tinnitis		+
Poor organisation		+
Food/chemical sensitivity		+
Poor sleep		+
Paranoia		+
Anxiety/panic attacks		+
Grandiosity/religiosity		+
Racing thoughts		+
Auditory hallucinations		+
Poor dream recall		+
Nervous		+

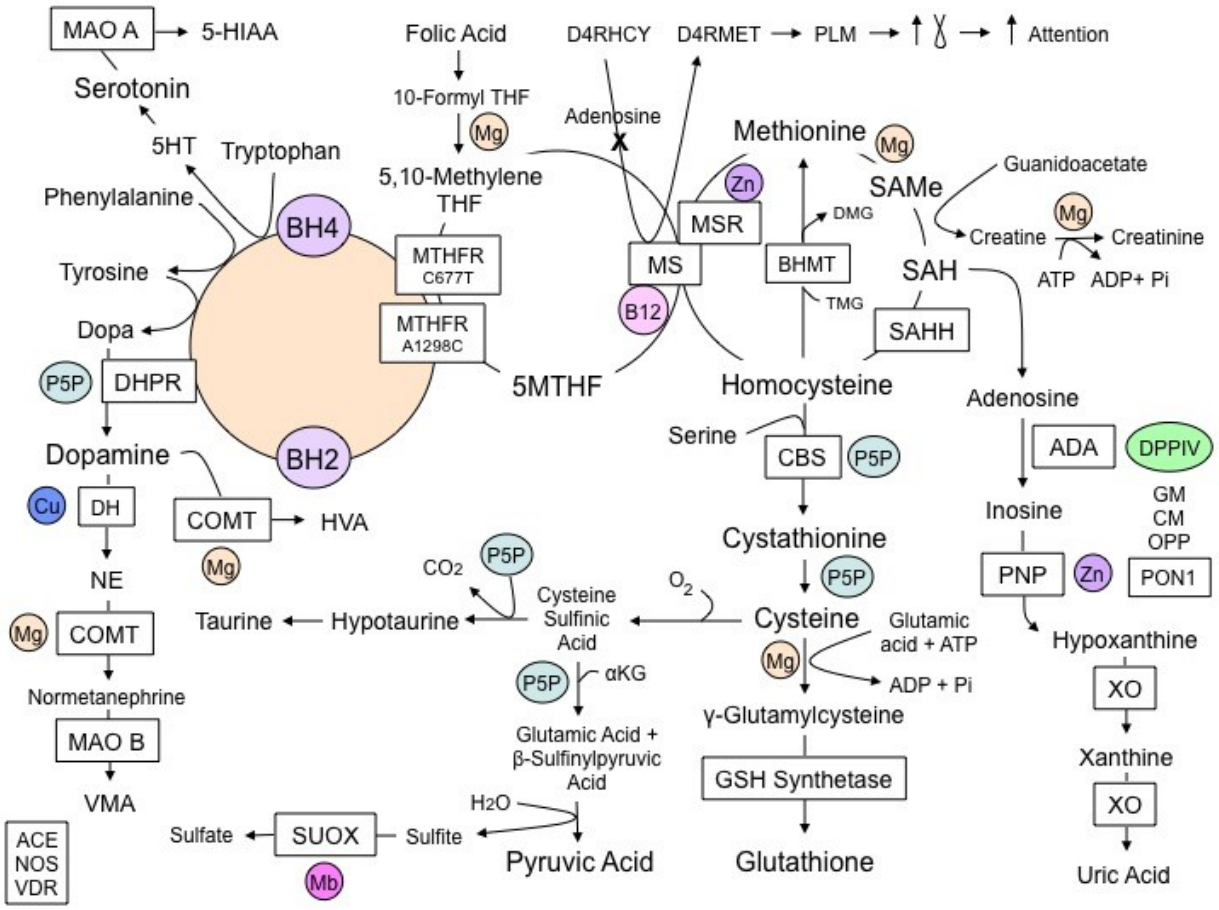
Some of the Signs and Symptoms that Methylation is impaired include:

- Diabetes
- Depression/Mood disorders
- Anxiety
- ADHD
- Premature Aging
- Suppress Immune System
- Digestive problems
- Fibromyalgia/Chronic Fatigue Syndrome
- Miscarriages, fertility, and problems in pregnancy
- Cardiovascular disease
- Cancer
- Addictive Behavior, including alcoholism
- Insomnia
- Autism and other spectrum disorders
- Bipolar or manic depression
- Allergies or Multiple Chemical Sensitivities
- Atherosclerosis
- Multiple Sclerosis and other Autoimmune Disorders
- Hashimoto's or Hypothyroidism
- Parkinson's
- Dementia/Alzheimer's
- Neuropathy
- Chronic Viral Infections
- Low T cells or reduced NK cells
- Sensitivity to medications



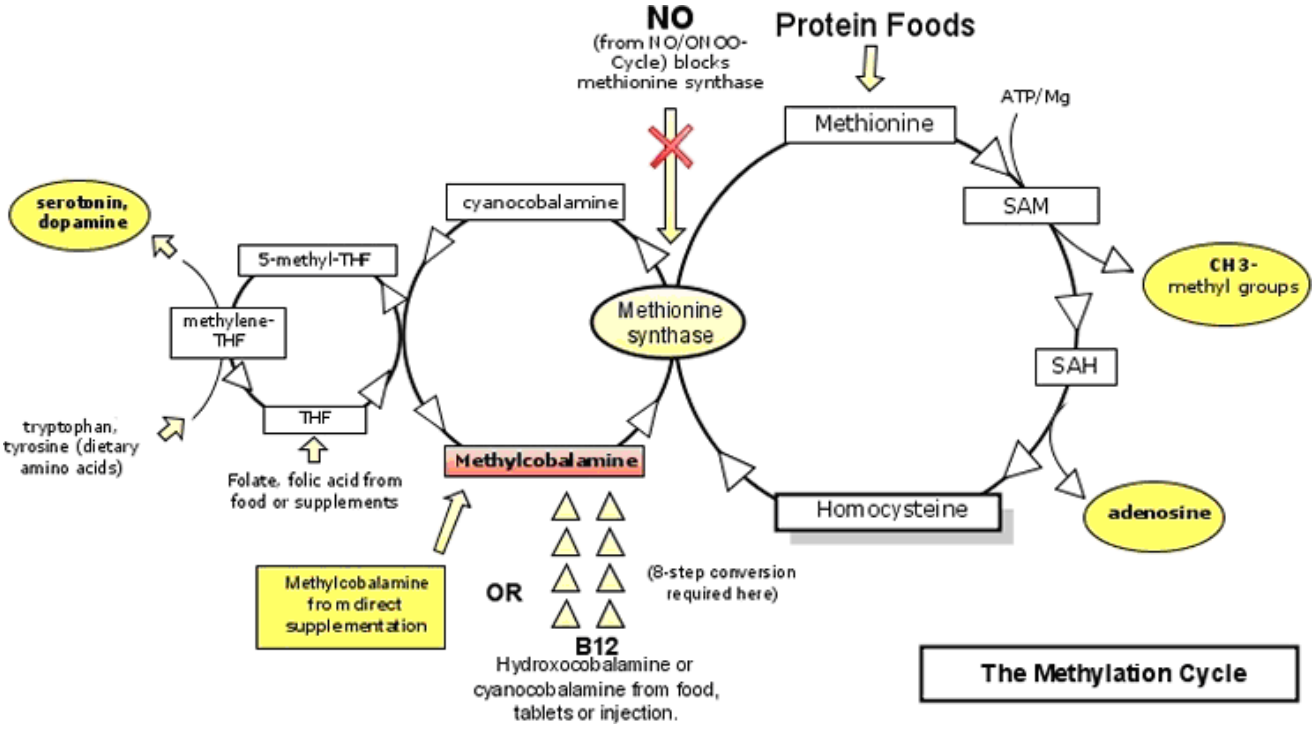
Above: In this rather "busy" diagram, the coloured rectangular boxes indicate where some of the genetic mutations may occur that can affect the methylation pathway.

Below: This diagram shows the importance of having adequate nutrients in place to make the pathways work and where active forms of supplements can be added to bypass "blocks" in the pathway due to gene mutations.



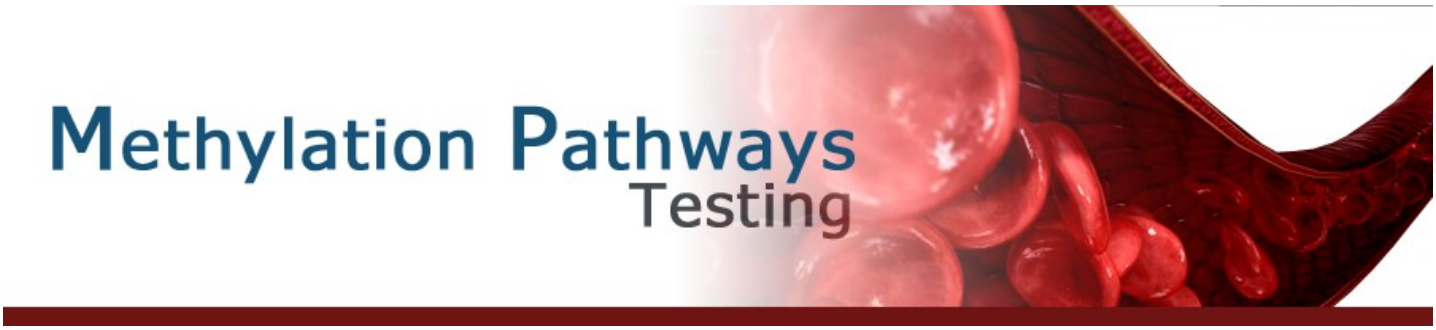
Methylation and Environmental Triggers

As an example of how an environmental trigger can affect methylation, it is not unusual to hear of autistic children, when subjected to the anaesthetic, nitric oxide, react very badly afterwards. The levels of various metabolites of the methylation pathway are important for protection from side effects of anaesthesia. As early as 1942 it was recognized that the addition of the amino acid, methionine, prevents the side effects due to the use of chloroform. Methionine affords protection from liver injury as a result of chloroform anaesthesia. Methionine also protects against effects of nitrous oxide anaesthesia. Nitrous oxide (NO) disrupts the activity of methionine synthase, a central enzyme in the methylation cycle (See the diagram below). Again, preloading with methionine appears to accelerate recovery and reduce side effects associated with this form of anaesthesia.



Drugs to Avoid with MTHFR Patients

- **Antacids** – PPIs, H2 blockers – can deplete B12
- **Cholestyramine and Colestipol** (+ fenofibrates) – decrease B12 and folate absorption
- **Methotrexate** – inhibits DHFR
- **Nitrous Oxide** – inactivates MS
- **Niacin** – depletes SAMe and inhibits pyridoxal kinase – active B6
- **Theophylline** – inhibits pyridoxal kinase
- **Metformin** – may decrease B12 absorption
- **Phenytoin and Carbamazepine** – antagonize folate
- **OCPs** – deplete folate
- **Trimethoprim or Bactrim** – inhibit DHFR
- **Sulfasalazine (Azulfadine) and Triamterene** – inhibit DHFR
- **Ethanol** - decreases folate intake, raises tHcy (in C677T)



How do we test for methylation status?

Gene Testing

Genetic tests look for single nucleotide polymorphisms or SNPs that alter the genes enough to affect certain biochemical processes, such as, methionine metabolism, detoxification, hormone imbalances, and folate metabolism. These are often incorporated into personalised genetic profile testing or testing for specific SNPs, like MTHFR can be done. With some of these gene tests it is important to be aware that although this is your genetic predisposition, often there are environmental triggers that need to be identified and either eliminated or treated, rather than just supporting the genetic weakness. These tests may be done via blood or saliva (depending on the SNPs being tested for).

Blood Tests

To see how effectively the methylation pathway is working, blood tests are available that measure individual metabolites in the pathway. For example there are blood tests that measure metabolites in the different pathways, some of these metabolites include:

Methylation Metabolism Biomarkers: S-adenosyl methionine (SAMe), S-adenosyl homocysteine (SAH), SAMe: SAH ratio, 5-methyltetrahydrofolate (5-MTHF), folinic acid tetrahydrofolate (THF).

Folate Metabolism Biomarkers: 5-methyltetrahydrofolate (5-MTHF), folinic acid, tetrahydrofolate (THF), active vitamin B12, red cell folate, homocysteine.

Methionine Metabolism Biomarkers: S-adenosyl methionine (SAMe), S-adenosyl homocysteine (SAH), SAMe: SAH ratio, active vitamin B12, red cell folate, homocysteine, methionine

Simple blood work via a general pathology can also be useful. Tests for homocysteine, folate, vitamin B12, histamine, basophils, etc., can be useful indicators. Sometimes starting with the simple tests before doing very specific testing is a good way to go.

Additional testing

If environmental triggers are suspected then specific testing for heavy metals, environmental pollutants, infections and inflammatory markers may also be useful.

Testing for adequate co-factors, vitamin B6, zinc, magnesium, copper, etc., is also a useful diagnostic tool.

Testing for pyrroluria may be useful as this condition depletes vitamin B6 and zinc.