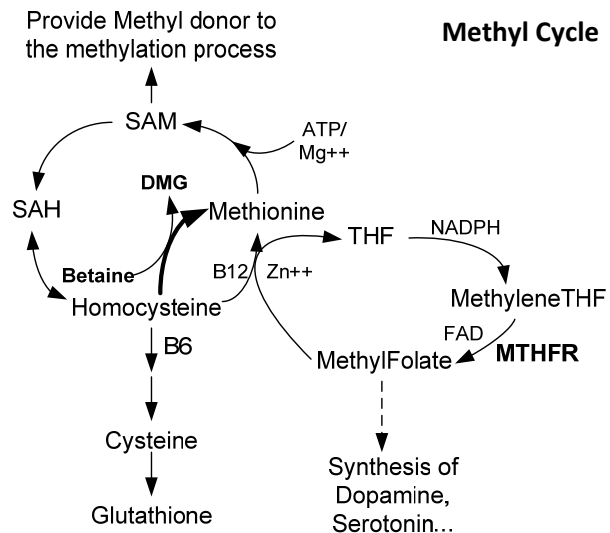


Methylation is a biochemical process of transferring of a methyl group (-CH<sub>3</sub>) from methyl donor onto other biological components such as DNA, protein and other molecules. Methyl Cycle refers to the pathway involving a series of enzymatic reaction that catalyze the regeneration of methyl donor to ensure the continuation of the methylation process. The Methyl Cycle is the backbone of our physiology that is carried in every cell and tissue to regulate healing, cell energy, genetic expression of DNA, neurological function, liver detoxification, immunity, and many other important functions.

Among these multiple enzyme reactions, MTHFR catalyzes the formation of methylfolate which is required for the recycling of homocysteine is a rate-limiting step. Genetic mutations of MTHFR, stress response, vitamins deficiencies such as B<sub>6</sub>, B<sub>12</sub>, and folate deficiency, can decrease the formation of methyl donor causing insufficient methylation with the accumulation homocysteine. When the homocysteine level is increased, it is rapidly metabolized back to SAH, which is a strong inhibitor of all reactions in the methyl cycle, causing further reduction of the methylation function, a vicious circle.



Reduced methylation function can affect over

200 types of methylation processes including biosynthesis of monoamine neurotransmitters such as dopamine and serotonin in the brain, detoxification of water insoluble toxins (especially in the liver), inactive cancer and virus genes, removal of histamine, synthesis of Co-Enzyme Q10 and carnitine which are required for ATP production (especially important for the heart). Elevated homocysteine can also cause injury to the important organs such as heart, liver, kidney and blood vessels due to its modification of cellular structures. Depending on the strength of other organs functions, one or more impairments can be developed. Common conditions associated with the poor methylation function include autism, decreased cognition, anxiety attacks, chronic fatigue, cancer, psychiatric disorders, myocarditis, sleep disorders, recurrent miscarriages, varicose veins, or autoimmune conditions etc.

### 1) MTHFR and Regulation of Its Enzymatic Activity

The rate-limiting step of the methyl cycle is the formation of methylfolate which is catalyzed by MTHFR. In the MTHFR gene, at least 40 mutations have been identified and the enzyme activity has been reduced significantly in these mutant forms. Two of the most investigated forms are C677T and A1298C with single nucleotide change. In heterozygous\* C677T, the MTHFR function is 40% reduced. In homozygous\* C677T, the MTHFR function is 70% reduced. In heterozygous\* A1298C, MTHFR function is 15% reduced and in homozygous\* A1298C MTHFR function is 30% reduced.

Adrenaline released from the adrenal glands can cause cAMP dependent phosphorylation which can reduce the catabolic activity of a series of enzymes involved in the basic metabolic function supporting processes such as growth, healing, reproduction etc. MTHFR is among the enzyme which is phosphorylated resulting in a 20% reduction of the enzyme activity. The phosphorylated MTHFR is more susceptible to SAH inhibition leading to further reduction of the enzyme activities. Such cAMP dependent enzyme phosphorylation activity refers as liver heat in TCM. People who have genetic mutations of MTHFR are more vulnerable to stress induced inhibition of MTHFR because their optimal activity is lower. Treatment that down regulates the stress responses, including the adrenaline release and the adrenaline stimulated cAMP dependent activities, will help keep the MTHFR functioning at an optimal level to maintain the regular methylation function.

Wei Lab's Hepavin Formula helps quench the cellular cAMP dependent response to the adrenalin stimulation by removing liver heat. It helps the liver and other tissues to relieve the inhibition of

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MTHFR so that the normal methyl cycle can be resumed.

## **2) Adrenaline and Stress Response**

Mental and physical stress including infections such as UTI, diseases such as kidney stones, pressure from work like facing dead lines cause an increase of adrenaline synthesis and secretion, referred as kidney heat in TCM. Controlling the adrenaline release from the adrenal gland can help lower stress related cAMP dependent MTHFR phosphorylation and associated enzyme activity inhibition. Wei Lab's KS Formula helps remove kidney heat. Used in combination with LC Balancer, it helps reduce adrenaline synthesis and secretion.

## **3) Methylation and Brain Function**

Methylation is a key step in the synthesis of monoamine neurotransmitters including serotonin, dopamine and melatonin which are involved in basic brain activities and play a crucial role in arousal, emotion and cognition. Lack of methylfolate formation can lead to deficiencies resulting in impaired brain function. Inside the brain, in addition to the basic neurons that take care of arousal, emotion and cognition, there are other types of neurons that control the activity of these basic neurons. The excitatory neuron which uses Glutamate as a neuron transmitter for example can stimulate the activity of the basic neurons. The inhibitory neuron which uses GABA as a neuron transmitter for example can exert an inhibitory effects to the basic neuron. Balance of the excitation and inhibition are important for healthy brain activity. When the basic neuron has difficulty releasing the desired amount of neuron transmitters, the control neuron will release more neurotransmitters to further stimulate the basic neuron, which can result in imbalanced excitation and inhibition and can cause a variety of disorders including mood swings, migraines, sleep disorders, depression, seizure, bipolar, or OCD (obsessive compulsive disorders) depending which direction the balance has tilted towards.

The brains over excitatory and inhibitory activity is referred as brain heat in TCM. The Platinum Formula helps reduce the excessive level of excitatory and inhibitory activity by removing the brain heat.

## **4) Methylation and Cardiovascular Function**

The synthesis of CoQ10 and carnitine in the body requires methylation and both CoQ10 and carnitine are the cofactors required in the ATP synthesis inside the mitochondria. Blockage of the ATP production in response to stress with elevated homocysteine levels are very damaging to the heart and blood vessels resulting in anxiety attack, arrhythmia, atrial fibrillation, tachycardia, bradycardia, angina, congestive heart failure, atherosclerosis, spider veins and phlebitis.

Arrhythmia and atrial fibrillation are due to the irregular function of the heart nerve due to the disturbance of the unsympathetic nerve activity by the sympathetic nerve in response to stress. Wei Lab's PaceKeeping Formula helps resolve the condition by nurturing the unsympathetic nerve and calming the sympathetic nerve in the heart. Anxiety attack, bradycardia (slow heart beat) and myocarditis is due to heart muscle weakness, heart Yang deficiency in TCM. Wei Lab's Myogen Formula nurtures the heart muscle and improves its strength by enhancing the heart Yang. Tachycardia is due to lack of muscle mass, heart Yin deficiency in TCM. Wei Lab's Millennium Formula provide hormonal support to help build the muscle mass by nurturing heart Yin. Angina, congestive heart failure, and atherosclerosis are caused by the lack of blood supply to the heart muscle due to narrowing of the coronary artery. Wei Lab's CV Formula helps resolve these conditions by boosting Qi, nurturing blood and liver, and increasing blood flow, blood oxygenation and blood quality. Spider veins, varicous veins and phlebitis are due to inflammation of the blood vessels, heat in the blood vessel in TCM. Wei Lab's Enlighten formula in combination with the Blood Tonic helps reduce the inflammation by removing blood vessel heat. These formulas help relieve the negative effects of poor methylation and high homocysteine level to the cardiovascular system.

## **5) Vitamin and Minerals in the Methylation Process**

Vitamin B<sub>12</sub> is the coenzyme required for methionine synthase to convert homocysteine to methionine using the methyl group from methylfolate. Normally, about 50% of homocysteine is remethylated and the remaining homocysteine is transsulfurated to cysteine which requires vitamin B<sub>6</sub> as a co-factor. This pathway yields cysteine, which is then used by the body to make glutathione, a powerful antioxidant that protects cellular components against oxidative damage. Deficiencies in vitamins B<sub>6</sub>, B<sub>12</sub>, and folate, can negatively affect the methylation process and cause high homocysteine levels.

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Most Vitamin deficiencies can be resolved by taking a vitamin supplement. However, the absorption of B<sub>12</sub> is very special. Digestion and absorption of B<sub>12</sub> is a very complex process and prone to mishaps leading to vitamin B<sub>12</sub> deficiency. Protein-bound vitamin B<sub>12</sub> must be released from the proteins of the food particles by gastric acid. Antacid and acid-blocking medications (especially proton-pump inhibitors) can inhibit the release of B<sub>12</sub> from the food. Elderly people who produce less stomach acid as they age thereby have increased probability of B<sub>12</sub> deficiencies. After the B<sub>12</sub> is released from food, it has to be bound by an intrinsic factor produced by the stomach before it can be absorbed. Poor stomach health with less Intrinsic factor secretion can cause B<sub>12</sub> malabsorptions and deficiencies, a cold stomach condition in TCM.

Wei Lab's GI solution including Spring Juice, Spring Capsule, Pearl Capsule and Formula B helps nurture the stomach to improve the digestion and absorption of vitamin B<sub>12</sub> by restoring the stomach lining and improving the blood supply and contractions.

In addition to Folate, Vitamin B<sub>6</sub> and B<sub>12</sub>, and several other vitamins and minerals are also required in the methylation process. Vitamin B<sub>2</sub> (FAD) helps recycle folate into a usable methyl-donor form. Vitamin B<sub>3</sub> maintains proper methylation of genes that suppresses tumor formation and growth. Vitamin C is also a cofactor for methylation enzymes. Zinc deficiency can lower the ability to use methyl groups from methyl donors causing hypo-methylation of DNA. Magnesium which combined with ATP is required for SAM synthesis from methionine. Several key enzymes needed for methylation reactions are copper dependent.

Although vitamin and mineral are important, over dosing can have toxic effects. Wei Lab's VitaLife has blended the well balanced and optimized amounts of vitamin, minerals, and other supplements with forty herbal ingredients to facilitate digestion and absorption. It exhibits superb benefits compared to other current available vitamin and mineral products.

#### **6) Liver/Kidney Function and Homocysteine By-pass**

In the kidney and liver, homocysteine is also remethylated by transferring a methyl group to homocysteine from betaine (trimethylglycine), a naturally occurring compound that can be found in food such as quinoa, spinach, beets etc. This process, only available in liver and kidney, can compensate for defects in the methylation cycle and help recycle the homocysteine to methionine when the regular pathway is not functioning well.

Eating plenty of vegetables to ensure enough supply of betaine, nurturing liver and kidney to boost the level of the catalytic enzyme and maximize the benefit of this by-pass can help reduce the homocystein level and enhance the methylation function. Wei Lab's Brown Formula helps nurture the liver structure and function by triggering the cGMP dependent biosynthesis of cellular components. The Qi Booster is also required if the patient also has low blood pressure or sugar levels, poor energy, chronic infections, acid reflux, or cancer, Qi deficiency in TCM. The LC Balancer improves kidney structure and enhances microcirculation by restoring the microcapillary structure of the glomerular and tubules and nurturing kidney Yin in TCM. The Xcel Formula improves kidney function and nurtures the adrenal gland by increasing the secretion of aldosterone and enhancing kidney Yang in TCM.

#### **Treatment Recommendations**

Depending on the patient's condition, the starting treatment can be the nurturing of the liver and kidney followed by removing heat, or vise versa, or rotating back and forth. If the patient presents with brain or heart related conditions, removing heat in combination with brain and heart related treatment is recommended as the starting treatment. When the patient's improvement plateaus or if the patient is not responding to the treatment, it is recommended to switch to the other type of treatment. Alternatively, when the heat removal is reaching the point where the patient feels exhausted, the liver and kidney nurturing treatment should be incorporated. Liver and kidney deficiency can be caused by degenerative changes due to aging or use of drugs. The deficiency and structure degeneration can also be caused by high homocysteine levels; the Yin is burned by the heat in TCM term.

\*Heterozygous = two different inherited genes (one inherited from each parent)

\*Homozygous = two of the same inherited genes (one each identical gene from each parent)