



# Healthy and Happy Monthly Newsletter

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## From the Womb to the Tomb, Folic Acid is an Essential Key to Ensuring a Successful Journey

In today's busy world it can be easy to overlook the symptoms of mineral nutrient deficiencies. Fortunately the body has ways of telling us that such imbalances exist. But as individuals most of us are unable to identify our body's cries for repair. We often take prescription and over the counter medications in order to manage the symptoms instead of addressing the root cause of the dysfunction, unaware that drug induced mineral/nutrient depletions may actually contribute to the resiliency of the disease. Not surprisingly, if the root cause of the symptoms is identified, addressing the message(s) that the body is trying to convey, the symptoms will cease to occur and the body will return to normal.

Folic acid has recently gained increased recognition in both the mainstream and complementary medical communities. From the weeks or even months before the moment of conception to the later stages of aging, the importance of folic acid exists in all phases of life. Similar to Vitamin C, humans are not able to synthesize folic acid, and so it is necessary to obtain it in supplement form or from the foods that we eat, especially fruits and vegetables. Would you be interested to know that while a folate deficiency has become less common in developed western society, lifestyle choices such as drinking, smoking, and poor diet, as well as certain prescription medications can increase the likelihood of developing a deficiency and lead to a number of health problems. If so, read on as we explore folic acid and the effect that it has on the body, influencing everything from DNA synthesis and cancer prevention, nerve damage and muscle weakness, mental function and cognitive decline, heart function, behavior, and more.

Otherwise known as Vitamin B9, folic acid is responsible for assisting in the healthy functioning of numerous bodily processes. As a member of the family of B Vitamins, folic acid aids the body to convert the carbohydrates that we take in as food into glucose which is used in all of the body's cells to produce energy. Therefore a deficiency in one or all of the B Vitamins can manifest with physical and emotional symptoms of low energy, muscle fatigue, brain fog, and increased irritability and anxiety.

The word folate is derived from the Latin word *folium*, which means leaf. There are four types of folic acid. Folic acid is the synthetic form of the nutrient which can be found in fortified foods and supplements. Folate is the natural form, which occurs in citrus fruits, leafy green vegetables and legumes like peas and beans. Folinic acid occurs in supplement form and is generally used in conjunction with cancer treatments. 5-MTHF (5-Methyltetrahydrofolate), the most bioactive form of folate, available in supplement form, is preferred by the body's cells for maximum absorption and also used in the brain, which we will discuss in more detail in the following paragraphs.

Most of us generally experience stress, fatigue, or low energy on a daily basis due to our modern high demand lifestyle(s), but we do not take into account the degree to which burning the wick from both ends can have on the future growth and human development of our offspring. But as we will see, a folic acid deficiency has the potential to be catastrophic for the new life that many of us hope to create. In fact, the signs and symptoms of folic acid deficiency in young children and adolescence may be more difficult to reverse after birth than if the parents took the steps to maintain adequate folate concentrations in the period before and during conception.



Having a healthy baby means taking the responsibility to make sure that you are healthy too. Men and women attempting to conceive need more folic acid in their bodies to lower the risk of neural tube defects in infants. These defects are a result of the abnormal development of the neural tube, the hollow structure in the embryo which precedes and develops into the brain and spinal cord. These neural tube defects most commonly result in malformations of the skull, spine and brain, including but not limited to cleft palate, spina bifida, and even brain damage.

While scientific research has long since confirmed the importance of folic acid in the normal development of DNA, the mechanisms of action for folic acid preventing birth defects are not fully understood and are still being studied. What we do know is that folate plays a major role in maintaining and helping to grow new cells, especially during periods of rapid cell division. This is why many OBGYNs and pediatricians encourage women to supplement with folic acid in the weeks preceding conception and during at least the first one to three months after conception to significantly reduce the risk of the fetus developing neural tube defects.



But it is not just women who need to be concerned with preventing a folic acid deficiency. For men, research indicates that in addition to zinc, adequate folic acid is important for reducing chromosomal sperm defects, and also fostering adequate sperm count. While a small percentage of a healthy male's sperm typically contain chromosomal abnormalities due to errors that occur during cell division in the testicles, like the female counterparts, the reason for this malfunction is still not fully understood. But researchers have now been able to conclude that adequate supplementation with folic acid in expectant fathers may help to reduce the incidence of miscarriages and birth defects like mental retardation and Down Syndrome.

For men and women trying to conceive a child, maintaining a healthy diet is of paramount importance to ensure adequate vitamin and mineral levels. Still, taking additional folic acid in supplement form may be necessary, especially if the mother or father has been regularly drinking alcohol and/or smoking before attempting to conceive. Smoking and drinking not only pulls water soluble vitamins and minerals like folic acid out of the body more quickly, but these unhealthy habits are stressful on the body which also causes these essential nutrients to be utilized more quickly by the body to produce the energy needed to deal with the trauma that partaking in these activities inflicts.

The minimum daily recommended intake for folic acid is 400mcg, although a higher amount may be necessary depending on the circumstances of the individual in question. Recognizing a dietary folate deficiency across our United States population, in 1996 the Food and Drug Administration published new regulations requiring that foods such as enriched breads, pastas, rice and other grain products be fortified with folic acid. While the intentions were sound, and the addition of folic acid in these foods is more beneficial than not, the fact remains that sugar and carbohydrate rich foods such as these further deplete the body of water soluble nutrients like B Vitamins and Vitamin C. Also, fortifying these foods with folic acid may make people more likely to rely on them for daily nutritional intake, but fails to take into account those who have gluten sensitivities, or the fact that regularly eating these foods can decrease mineral/nutrient absorption in the gut and increase developing Type 2 Diabetes due to the recurrent insulin spikes that occur from consuming them. Still, since folic acid foods have been integrated into western society and around the world, there has been a significant decrease in the incidence of infants born with neural tube defects.

Based on our modern nutritionally deficient western diet, dietary folate alone may not be enough to ensure proper fetal development in women and normal sperm development in men. Due to today's mineral and nutrient depleted soil from over farming, even eating more fruits and vegetables may not be enough, as our conventional produce is also comparatively poor in nutrition when compared to the produce that our grandparent's generation consumed during their child bearing years.

Be careful not to consume too much folic acid however, as some studies indicate that a high ratio of prenatal folic acid in conjunction with a low level of Vitamin B12 may predispose an unborn fetus to developing metabolic disorders like childhood obesity and heart disease, stroke, and Type 2 diabetes in adults. For this reason, it is important to consult with your doctor and pharmacist early on in the child planning stages to ensure that you are adequately and safely supplementing with folic acid and other essential nutrients in preparation for achieving a successful conception.

Another intense area of research is that too much or too little folic acid during in utero development may cause changes in brain development leading to Autism Spectrum Disorders (ASD). ASDs embody a wide range of symptoms from impaired motor skills, speech, emotional and social development, to gastrointestinal and mitochondrial disorders. These restrictive behaviors and dysfunctions can be moderate to severely disabling for the child. While it is true that folic acid plays a role in DNA synthesis and repair, and is important for proper fetal development and preventing genetic syndromes, studies have concluded that these genetic syndromes are only observed in a small percentage, less than 15%, of children with autism spectrum disorders. So for now, abnormalities of the DNA, or missing or extra chromosomes cannot be the only contributing factors to unlocking the mysteries of this human condition.

With further research in recent years there are also promising associations with ASDs and physiological abnormalities like gastrointestinal immune system dysfunction and resulting inflammation, mitochondrial insufficiencies, environmental toxin exposure, and the resulting cumulative oxidative stress that the body undergoes as a result of these factors. As more knowledge is accumulated on Autism Spectrum Disorders, researchers are discovering new disorders that can also influence or produce synergistic symptoms on the spectrum when coupled with other physiological factors. One of the most recent discoveries involving Autism Spectrum Disorders and folic acid is a disorder called Cerebral Folate Deficiency (CFD).

Cerebral Folate Deficiency is a manifestation of below normal levels of the active form of folate, known as 5-methyltetrahydrofolate (5-MTHF), in the central nervous system (brain), despite normal levels of folate metabolites in the blood outside of the central nervous system. Similar to symptoms on the Autism spectrum, children with CFD can exhibit difficulty walking, abnormal balance, speech problems, and other Autistic symptoms. It is through the process of determining why CFD occurs that researchers believe it is related to Autism Spectrum Disorders, but still not a direct cause. As we will see, mitochondrial dysfunction may be the link that couples the two disorders.

Folate is of paramount importance when it comes to a properly functioning methylation cycle. The methylation cycle is a biochemical pathway that manages a wide range of processes in the body. From maintaining proper detoxification and energy production, to controlling inflammation and regulating DNA, the methylation cycle helps the body to adjust and adapt to environmental stressors by repairing and rebuilding, keeping each and every cell functioning correctly.

It is important for the enzyme MTHFR (methylene tetrahydrofolate reductase) to work properly because it converts folate into 5-MTHF and directs it into the methylation cycle. There are genetic conditions where this enzyme does not function properly. Supplementing with the most active form 5-MTHF has been found to be beneficial in individuals with conditions related to the decreased enzyme activity. The question is why? Also, what if the enzyme is working properly and there is still a disruption in the methylation cycle?

Normally, folate is converted into 5-MTHF through a metabolic process, whereby it is then transported into the brain at a location called the corticoid plexus through one of two pathways. The first pathway is the folate receptor protein alpha (FRA), which is largely dependent on the mitochondria and ATP production. The other, is the reduced folate carrier (RFC).

In 2005 researchers discovered an autoantibody which attaches to the folate receptor protein alpha (FRA) and makes it dysfunctional. An autoantibody is a type of protein that is produced by the immune system and works against one of the body's own proteins. The cause of this happening is not completely understood, but it may be due to a genetic predisposition that is influenced by an environmental trigger, a concept known as epigenetics.

In the case of Cerebral Folate Deficiency, the FRA is highly attracted to folate metabolites as well as the antibodies that disrupt it. These antibodies can both bind permanently to or block the transport of folate metabolites like 5-MTHF across the blood brain barrier. As the main pathway, FRA does attract folate metabolites, but cannot take in a lot, which is why it is responsible for 5-MTHF transport across the blood brain barrier when folate metabolites are low outside of the cell. We are fortunate to have the second pathway, the reduced folate carrier.

The reduced folate carrier has a low attraction for 5-MTHF, but it has a high capacity and can take in a lot, which is why it is responsible for transporting folate metabolites across the blood brain barrier when concentrations in the blood are high. Unlike the FRA, the RFC can transport 5-MTHF in and out of the cell, it is not blocked by folate receptor autoantibodies, and it is not dependent on the mitochondria and ATP. The folate receptor protein alpha requires energy (ATP) to work, and this energy comes from the mitochondria. Many children with Autism Spectrum Disorder have mitochondrial insufficiency and so they produce less ATP, which may lead to less 5-MTHF in the brain. So, regardless of whether Autism Spectrum Disorder leads to Cerebral Folate Deficiency, or Cerebral Folate Deficiency exacerbates Autism Spectrum Disorder, in the case of both, symptoms can be improved and made more manageable by supplementing with 5-MTHF.

In addition to supplementing with 5-MTHF, it had also been found that removing cow's milk and cow's milk products from the diet of individuals with these disorders can improve symptoms. Cow's milk contains a FRA antigen that is 91% similar to the human antigen. Antigens are substances that produce an immune response by the body, especially the production of antibodies. In this case, autoantibodies to the folate protein receptor alpha react to the antigen in cow's milk and increase in concentration, leading to a worsening of symptoms. In several studies involving children with both Autism Spectrum Disorders and Cerebral Folate Deficiency, switching to a milk free diet as well as supplementing with 5-MTHF yielded statistically significant results where autoantibody concentrations were reduced and symptoms improved.

Folate has also been shown to be cardio (heart) and neuro (brain) protective. Cardiovascular disease is the number one killer of men and women in the United States today. The amino-acid homocysteine is produced in the body from methionine, usually as a byproduct of consuming meat. A higher concentration in the blood is associated with hardening or narrowing of the arteries (atherosclerosis), and an increased risk of heart attack, stroke, and blood clots.

Studies have shown that elevated homocysteine levels can lead to an endothelial dysfunction of the arteries, weakening the integrity of the vessels, which is an underlying cause of heart attacks. The endothelial layer is the inner level of cells that line the arteries. Fortunately, there is a good body of evidence that suggests that supplementing with folic acid can significantly lower blood levels of homocysteine by converting it back into methionine. In addition, folic acid appears to reverse the degenerative effects of endothelial dysfunction independent of its homocysteine lowering abilities. One reason may be that 5-MTHF can increase nitric oxide production and improve its bioavailability.

While nitric oxide has been the subject of thousands of studies and been shown to be involved with everything from memory and behavior, improving the quality of sleep, increasing endurance and strength, and reducing inflammation, it has drawn the most attention for its heart health benefits. The endothelial cells produce nitric acid. When plaque accumulates in the arteries, it lowers the ability of the cells to produce nitric acid. Nitric acid is a vasodilator that allows more blood flow and oxygen to get into cells and inhibits the buildup of plaque.

Folate's ability to protect the brain is similar to its ability to protect the heart, it has a profound effect on the viability of blood vessels. Therefore it is only logical to wonder if folic acid can be beneficial for individuals who experience frequent migraines. Several studies indicate that indeed, folate in the form of 5-MTHF can reduce the severity and duration of discomfort in migraine sufferers due to its ability to reduce homocysteine.

Researchers also suggest that the occurrence of migraines may be related to a genetically inherited trait, the MTHFR gene mutation that does not allow the body to convert folic acid into its active form 5-MTHF. Of the studies, several researchers tested migraine suffering participants for the MTHFR gene mutation, which is associated with higher homocysteine production, and found that a significant number of the migraine sufferers had the mutation. Also, one study found that individuals with frequent and severe migraines were more than four times as likely to have both the mutation and elevated levels of homocysteine. While the results of these studies have yet to be proven and more research is underway, the pathways and mechanisms of action by which all of this dysfunction occur seem to hold folic acid and the normalcy with which it is converted into its active form as a common denominator.

In addition, folate is believed to play an important role in cancer prevention. Similar to the above information, the method of action for why folate may help to prevent certain cancers is not fully understood. There is an incontrovertible inverse relationship between higher concentrations of folate metabolites and a reduced risk of colon, breast, cervical, and gastrointestinal cancers, however. It is also understood that there exists several complex mineral/nutrient interactions with DNA and gene expression. As a result there is a momentum behind researching all aspects of biochemical mechanics in order to gain a more complete picture of what causes these disease states so that hopefully less invasive and more effective treatments will be developed.

Many studies have explored and discovered substantial results related to the role of folate in the body for synthesizing important enzymes and compounds that are necessary for DNA replication and repair. Truthfully, there are several studies which show that folate may play a dual role in cancer. It may be beneficial in preventing the initiation of cancer formation, especially in individuals with a low folate level, but it may also hasten the growth of the cancer if taken after the disease is discovered. To date, the optimum intake for the prevention of certain cancers has yet to be established.

Since folic acid symptoms are also consistent with other deficiencies, if you are concerned with your mineral/nutrient status, your doctor can review your lifestyle and prescription drug use, and perform a simple blood test to measure your levels and determine if any inadequacies exist. The importance of folic acid cannot be diminished, but before you start mega dosing with any supplement, understand that it is important to carefully evaluate your situation with your doctor and pharmacist. There is no such thing as a one size fits all scenario, and like all things in life, more is not always better depending on the circumstances.