NATURE'S PATH
FAMILY WELLNESS

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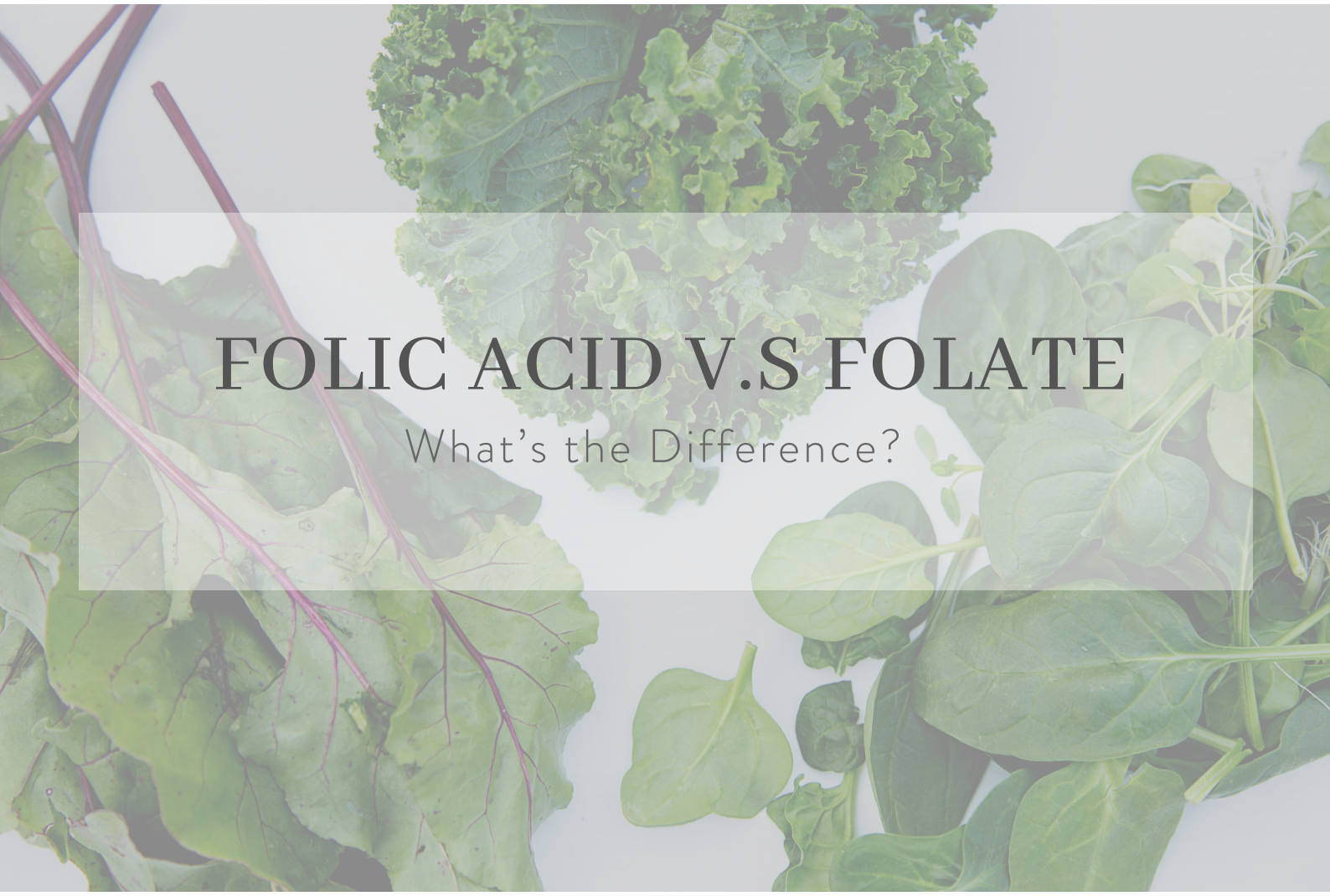

FOLIC ACID V.S FOLATE

What's the Difference?

IN THIS GUIDE

LETS TALK ABOUT VITAMIN B9

Understanding the differences between folate and folic acid can help you make choices that support fertility, pregnancy and overall health.

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BACKGROUND OF VITAMIN B9

What is Folate and why is it important?

Folate is the broad term to describe the various forms of Vitamin B9, an essential nutrient involved in many important physiologic processes.

Folate is needed to create every cell in the body, and it is used directly in the synthesis of DNA and neurotransmitters including dopamine, norepinephrine, epinephrine, and serotonin.

Folate has an important role in "Methylation Reactions." Methylation is involved in the following physiologic functions:

- Turning genes on and off (epigenetics)
- Breaking down chemicals, toxins, neurotransmitters, estrogen and histamine
- DNA synthesis (needed for repairing and regenerating cells and body tissue, and for growing a healthy fetus during pregnancy)
- Red blood cell production
- Energy Production
- Producing myelin for brain and nerve cell health
- Making phosphatidylcholine for cell membranes, and bile flow for fat absorption

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What is Folic Acid?

Folic acid is a synthetic form of B9, added to many supplements and processed foods containing enriched flour. Folic acid is not the same form of B9 that is found naturally in food (leafy greens, nuts, seeds, legumes). It is a synthetically manufactured substance that is difficult for most people to process. Unlike the folate found in food, folic acid needs to be transformed by the body's enzymes to become "active" and useable by the body. Unfortunately, our bodies have a limited capacity to process folic acid, which means that much of it remains unmetabolized and acts a like toxin in the body, increasing the risk of health concerns.

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FOLIC ACID CONCERNS

Health concerns related to excess folic acid:

- Folic acid can block methyl-folate (5-MTHF), the bioactive form of folate naturally found in food, from binding to folate receptors and transporters that carry folate into the cells where it is active.

- Individuals with genetic variants that slow folate breakdown are more negatively affected by excess folic acid. When folic acid is consumed by these individuals, it binds to the folate receptor, it is inefficiently broken down, and it blocks natural folate from binding to receptors adding to the compromised folate processing. Also, some genetic variants slow the enzyme DHFR which is needed to process folic acid. This results in an increased buildup of toxic folic acid and an increased risk of developing folate deficiency compromising all the methylation reactions listed above.

- Supplementing with folic acid can mask anemia caused by B12 deficiency, preventing individuals from getting diagnosed and treated.

- Unmetabolized folic acid is associated with reduced natural killer cell function, an immune cell that is our first line of defense in the prevention of cancer and viral infections.

- Folic acid supplementation during pregnancy and fetal exposure has been associated with an increased risk of respiratory illness in children. Unmetabolized folic acid has also been detected in newborn babies and in 4-day-old formula-fed infants.

- Folic acid is more vulnerable to degradation by UV radiation than methyl-folate, therefore people who live in sunnier climates or have fair skin may have an increased risk of developing folate deficiency if they are supplementing with folic acid.

- The take home message is that folic acid is synthetic, acts like a toxin, and can be harmful to most people even at moderate doses.

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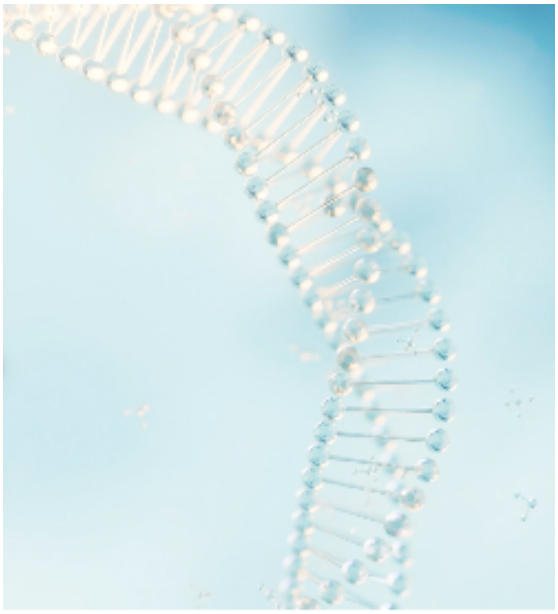
GENETIC VARIANTS & FOLATE PROCESSING

Folate and Genetic Variants:



- More than a 1/3rd of the US population carries a genetic variant or Single Nucleotide Polymorphism a.k.a "SNP," that slows the enzymes that process folic acid and folate in the body.

- Some ethnic groups have higher rates of these SNPS, particularly people of Latin American, Native American, Caucasian, and Asian descent, with the highest frequency (47%) seen in the Latin American population.

- The folate-related genes include: DHFR, MTHFD1, MTHFR, MTRR and MTR, FOLR1, FOLR2, SLC19A1, MTHFS, and SHMT. MTHFR is the most well-known and researched gene.

MTHFR and Folate

Individuals with SNPs in their MTHFR gene can have almost 75% less available active folate (5-MTHF) due to having a slow acting MTHFR enzyme. On bloodwork, these individuals may have low red blood cells, low intracellular folate and elevated homocysteine (a player in cardiovascular disease). Homocysteine requires folate to be broken down. If folate is deficient, homocysteine will become elevated, increasing the risk of heart disease.

- These folks may experience problems with folic acid supplementation because they inherently don't process folic acid well and folic acid further blocks the binding of natural folate to the cell's folate receptors. Therefore, people with the MTHFR SNP (and the other folate related SNPS listed above) should avoid fortified foods, enriched flour, and folic acid.

- They may also benefit from supplementing with small doses of 5-MTHF (methylene tetrahydrofolate) and calcium folinate. Supplementing with 5-MTHF is more effective than folic acid at improving folate levels in people with and without MTHFR SNPs.

- They should also eat plenty of natural folate containing foods such as leafy greens, nuts, seeds, liver, and legumes.

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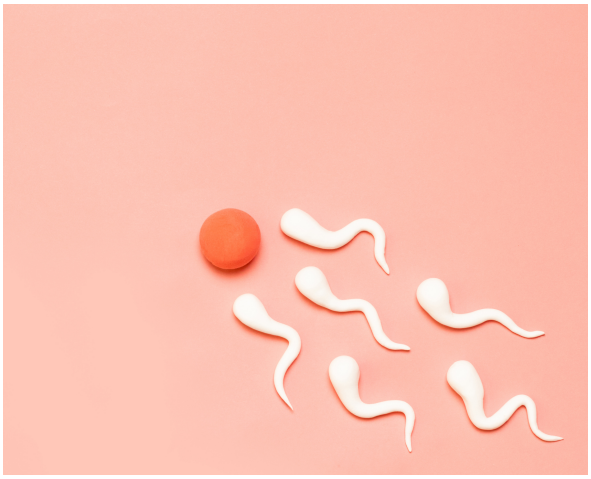
FOLATE & REPRODUCTIVE HEALTH

Fertility and Folate

▪ Having a MTHFR genetic variant and subsequent low folate levels are associated with fertility challenges. This SNP can compromise sperm and egg cell's roles in healthy conception.

▪ Both male and female carriers of MTHFR SNPs have increased risk of miscarriage.

▪ Couples that struggle with fertility have increased rates of MTHFR SNPs.



Pregnancy and Folate

Adequate folate levels during early pregnancy are essential for healthy neurological development of the fetus and placental growth.
Folate supplementation is recommended during pregnancy to prevent neural tube defects (defects in the brain, spine and spinal cord) in a developing fetus, and other birth defects like congenital heart defects and orofacial clefts. Additionally, healthy folate levels have an inverse relationship with low birth weight and preterm birth, suggesting that it decreases the risk of both.

- SNPs that affect Folate processing may increase the risk of preeclampsia, HELLP Syndrome, eclampsia, uteroplacental insufficiency, intrauterine growth restriction, recurrent pregnancy loss, gestational hypertension, placental abruption, Neural tube defects and Down Syndrome.
  - Supplementing with methyl folate may reduce the risk of recurrent preeclampsia for a woman who experienced preeclampsia in a past pregnancy.

- Preconception levels of serum folate are important because folate drops during pregnancy and it usually takes 2-3 months of supplementation before achieving optimal folate levels.
  - For this reason we recommend supplementing at least 400 mcg of 5-MTHF at least 12 weeks before trying to conceive and continue supplementation until at least 12 weeks after conception to reduce the risk of neural tube defects.
- After delivery of the baby, supplementation of methyl-folate has been shown to keep maternal folate levels stable better than folic acid supplementation.

Food Sources of Folate

- Fresh green leafy vegetables
- Legumes: Lentils, chickpeas, pinto beans, black-eye peas, black beans, edamame, tofu
- Avocados, asparagus, broccoli, sprouts, beets
- Non-fortified brewer's yeast
- Liver and kidney
- Nuts and seeds
- Fruits: oranges, papaya, mango, pomegranate, kiwi, strawberry

Food for Thought

The main argument against supplementing with 5-MTHF (instead of folic acid) is that studies show supplementing with folic acid while pregnant decreases the risk of neural tube defects (NTDs) in a fetus, while no studies have been conducted to demonstrate whether 5-MTHF can also prevent neural tube defects.

Studies using 5-MTHF supplementation in pregnancy have not been conducted because it is unethical to perform research studies on pregnant women.

However, we know that 5-MTHF supplementation increases folate levels more than folic acid (at 3 months) and since folate levels are the key determinant for assessing nutritional risk of NTDs, we can assume that 5-MTHF supplementation can protect against NTDS by the same mechanism that folic acid does, by raising folate levels in the blood. And since 5-MTHF carries less risk than folic acid (i.e unmetabolized folate, masking B12 deficiency, harmful with genetic variants), we recommend replacing all folic acid supplementation with natural folate containing foods, calcium folinate, or methylated folate (5-MTHR).

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