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UNDERSTANDING THE MTHFR GENETIC VARIANT AND HOW TO SUPPORT IT (2026 UPDATE)

Methylenetetrahydrofolate reductase (MTHFR) is an enzyme that plays a critical role in methylation, a foundational biochemical process required for DNA synthesis, detoxification, hormone metabolism, neurotransmitter production, mitochondrial function, and cellular repair. Genetic variants in the MTHFR gene can reduce enzyme efficiency and influence how the body processes folate and regulates homocysteine levels.

MTHFR variants are extremely common:
- 30 to 40 percent of the population carries one copy of C677T
- 10 to 15 percent carries two copies
- Up to 60 percent carries at least one MTHFR variant

In clinical practice, reduced MTHFR function most commonly impacts:
- Fertility and pregnancy outcomes
- Egg and sperm quality
- Recurrent pregnancy loss
- Thyroid function
- Detoxification capacity
- Immune balance
- Neurotransmitter function

You can identify your MTHFR status through:
- Physician-ordered genetic testing
- Direct-to-consumer testing such as 23andMe
- Functional lab markers, especially homocysteine

Having an MTHFR variant does NOT mean disease is inevitable. It simply means your body may require more targeted nutritional and metabolic support.

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THE TWO MOST COMMON MTHFR VARIANTS

There are many MTHFR polymorphisms, but two account for most clinical relevance.

MTHFR C677T

This variant reduces the enzyme's ability to convert folate into its active form, 5-MTHF.

Estimated reduction in enzyme function:
- Heterozygous: approximately 30 to 40 percent reduction
- Homozygous: approximately 60 to 70 percent reduction
- Compound heterozygous: approximately 40 to 60 percent reduction

Possible clinical impacts:
- Elevated homocysteine
- Increased oxidative stress
- Impaired DNA repair
- Reduced egg and sperm DNA integrity
- Increased miscarriage risk
- Reduced detoxification capacity

MTHFR A1298C

This variant affects production of tetrahydrobiopterin (BH4), which supports neurotransmitters, nitric oxide production, mitochondrial function, and vascular health.

Possible impacts:
- Neurotransmitter imbalance
- Sleep disturbances
- Reduced mitochondrial efficiency
- Vascular function changes
- Fertility challenges related to mitochondrial or vascular health

Homocysteine is often normal with isolated A1298C.

WHY I STEER CLEAR OF FOLIC ACID
Folic acid is the synthetic form of folate. You'll find it in most conventional prenatal vitamins and in fortified foods like cereal, bread, and pasta. Here's the thing: your body can't use folic acid as is. It first has to be converted by an enzyme called DHFR. Research on human liver tissue found that this enzyme works extremely slowly and varies a lot from person to person. When you take in more folic acid than your body can convert, it ends up circulating in your blood as unmetabolized folic acid. To be clear, people with MTHFR variants can still process folic acid. But since the conversion is slow for everyone, I'd rather give your body folate in forms it can use right away: methylfolate (5-MTHF) in your supplements, plus real food folate from leafy greens, lentils, asparagus, avocado, and liver. That's why I recommend skipping supplements and foods fortified with folic acid.
References: Bailey SW, Ayling JE. PNAS 2009. PMID 19706381. CDC, MTHFR Gene Variant and Folic Acid Facts.

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WHY MTHFR MATTERS FOR FERTILITY

Methylation is essential for:

- Egg DNA integrity
- Sperm DNA stability
- Embryo development
- Implantation
- Placental formation
- Mitochondrial function

Reduced methylation efficiency has been associated with:

- Recurrent pregnancy loss
- Poor embryo quality
- Reduced sperm quality
- Fertility challenges (PMID: 28842818, 32478379, 33914208)

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EVIDENCE-BASED SUPPORT STRATEGIES FOR INDIVIDUALS WITH MTHFR VARIANTS

Prioritize natural folate intake
Best food sources include:
• Spinach
• Arugula
• Romaine lettuce
• Asparagus
• Broccoli
• Avocado
• Beets
• Lentils
• Grass-fed liver
Aim to consume multiple servings daily.

Supplement with methylated folate when appropriate
Biologically active forms include:
• L-5-methyltetrahydrofolate
• Levomefolate
• Metafolin
• Quatrefolic

Recommended dosing for fertility and pregnancy:
• 1 mg to 1.7 mg daily (1,000 to 1,700 mcg), depending on individual needs

Additional important option:
• Folinic acid (5-formyltetrahydrofolate) is another excellent form of folate
• Supports DNA synthesis and cellular function
• Often better tolerated in individuals sensitive to methyl donors
• May be used alone or alongside methylfolate depending on individual biochemistry
Folic acid
• Folic acid is synthetic and requires MTHFR conversion
• Individuals with MTHFR variants may accumulate unmetabolized folic acid
• Many supplements contain BOTH methylfolate and folic acid — these should be avoided entirely
• Always choose supplements containing methylfolate and/or folinic acid ONLY

All of my recommended fertility supplements that meet these criteria can be found at: AimeeRaupp.com/FertilitySupplements

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Support choline intake
Choline provides an alternative methylation pathway independent of MTHFR and is essential for egg quality, fetal brain development, and placental health (PMID: 20220206).

Best sources include:
• Egg yolks
• Liver
• Grass-fed meats
• Salmon
• Sunflower lecithin

Optimize vitamin B12 status
Vitamin B12 works directly with folate in methylation.
Preferred forms:

• Methylcobalamin
• Hydroxocobalamin
• Adenosylcobalamin

Optimal fertility levels are generally above 500 pg/mL.

Support homocysteine metabolism
Homocysteine is a key functional marker of methylation.
Optimal fertility range:
• 5 to 8 µmol/L

Supportive nutrients include:
• Methylfolate
• Folinic acid
• Vitamin B12
• Vitamin B6
• Riboflavin (B2)
• Choline
• Betaine (also called trimethylglycine or TMG) lowered homocysteine in a clinical trial; fertility outcomes were not measured (PMID: 12730412).

Support mitochondrial health
Methylation directly influences mitochondrial function and cellular energy production.

Helpful nutrients include:
• CoQ10
• Magnesium
• Glycine
• NAC
• Selenium

Eat adequate protein
Protein provides amino acids required for methylation and detoxification.

Recommended intake:
• 0.6 to 0.8 grams per pound of body weight daily

Support detoxification pathways
Support detoxification through:
• Regular exercise
• Sauna therapy
• Adequate hydration
• Cruciferous vegetables
• Collagen and bone broth

Avoid folate-blocking or folate-depleting medications when possible
These may include:
• Methotrexate
• Proton pump inhibitors
• Certain hormonal contraceptives

Always consult your physician before stopping medications.

IMPORTANT CLINICAL PERSPECTIVE

MTHFR variants do not determine your fertility outcome. What matters most is how effectively methylation is functioning. Functional markers such as homocysteine, B12, and folate levels provide more meaningful clinical insight than genetics alone. With proper nutritional and metabolic support, methylation pathways can function optimally and support healthy egg quality, sperm quality, and pregnancy outcomes.

If you would like individualized guidance, my team and I offer comprehensive fertility coaching and functional testing support to help optimize methylation, fertility, and overall reproductive health based on your unique biochemistry.

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MEDICAL RESEARCH LINKING MTHFR AND FERTILITY

- **MTHFR and embryonic development**
https://pubmed.ncbi.nlm.nih.gov/32767205/

- **Paternal MTHFR deficiency and reproductive decline**
https://pubmed.ncbi.nlm.nih.gov/34128976/

- **MTHFR polymorphisms and recurrent pregnancy loss**
https://pubmed.ncbi.nlm.nih.gov/32478379/

- **MTHFR polymorphisms and sperm DNA integrity**
https://pubmed.ncbi.nlm.nih.gov/28842818/

- **Folate metabolism and female fertility**
https://pubmed.ncbi.nlm.nih.gov/20137055/

- **MTHFR variants and methylation in fertility patients**
https://pubmed.ncbi.nlm.nih.gov/33914208/

- **5-MTHF versus folic acid in pregnancy outcomes**
https://pubmed.ncbi.nlm.nih.gov/29882091/

- **Meta-analysis: MTHFR variants associated with recurrent pregnancy loss**
https://pubmed.ncbi.nlm.nih.gov/37248348/

- **Meta-analysis: MTHFR polymorphisms and male fertility**
https://pubmed.ncbi.nlm.nih.gov/32912251/

- **Choline requirements influenced by MTHFR genotype**
https://pubmed.ncbi.nlm.nih.gov/20220206/

- **Riboflavin lowered homocysteine in adults with the MTHFR 677TT genotype**
https://pubmed.ncbi.nlm.nih.gov/16380544/

- **Dietary folate and assisted reproduction outcomes (observational study)**
https://pubmed.ncbi.nlm.nih.gov/25198264/