



MTHFR Genetic Mutations

What is MTHFR?

MTHFR (Methylenetetrahydrofolate Reductase) is a gene that helps your body process folate (vitamin B9) and convert it into its active form, **methylfolate**. Methylfolate is important for many functions in the body, including:

- DNA repair and production
- Healthy pregnancy and fetal development
- Detoxification pathways
- Neurotransmitter production (serotonin, dopamine, norepinephrine)
- Energy production
- Cardiovascular health
- Homocysteine metabolism

Why Does MTHFR Matter?

When MTHFR activity is reduced, some people may have difficulty converting folic acid and folate into the active form methylfolate.

Potential consequences may include:

- Elevated homocysteine levels
- Fatigue
- Brain fog
- Mood changes
- Difficulty with detoxification pathways
- Increased nutrient needs
- Pregnancy complications in some individuals

What is an MTHFR Mutation?

- An MTHFR mutation is a common genetic variant that can reduce the efficiency of the MTHFR enzyme
- In the U.S., 1 in 3 people have at least one MTHFR variant, and 1 in 10 have variants in both gene copies
- MTHFR variants may lead to low folate and B vitamin levels and higher blood homocysteine levels, which can be associated with various health concerns
- Having an MTHFR variant does **not** mean you have a disease. Many people with MTHFR variants are healthy and never experience symptoms.
- **Two common variants in the MTHFR gene are C677T and A1298C**
- You can have one copy of a variant = HETEROZYGOUS
- Or two copies = HOMOZYGOUS

C677T HETEROZYGOUS • ~35-40% decrease in enzyme effect • "Thermolabile" enzyme; more sensitive to low folate	C677T HOMOZYGOUS • ~70-80% decrease in enzyme effect • Strongest impact on folate-dependent methylation
A1298C HETEROZYGOUS • Slight decrease in enzyme effect • Mild effect on its own	A1298C HOMOZYGOUS • ~20% decrease in enzyme effect

You can also be heterozygous for both variants which causes ~50% decrease in enzyme effect

Homocysteine

- Amino acid that converts to methionine via methylation to support several biological processes
- With MTHFR variants, conversion may be incomplete, and homocysteine can accumulate
- High levels can damage blood vessel linings & increase risk of blood clots, heart attacks, strokes, cognitive decline, & bone loss

Treatment for MTHFR Variants (and elevated homocysteine when present)

- Methyl folate supplementation
- Avoid "folic acid" supplements - This non-methylated folate may not be fully processed and can accumulate
- Increase folate in diet - Beef or chicken liver, spinach, leafy green vegetables
- Supplementation of B vitamins as needed based on labs and symptoms
- Avoid alcohol & smoking - These deplete B vitamins and inhibit methylation
- Physical exercise - Supports methylation and cardiovascular health
- Choline - Supports methylation and homocysteine management; Found in beef or chicken liver and eggs