Basic information about the

MTHFR Gene

MTHFR testing is unnecessary.

Why? *Many people have one or two genetic variants in the MTHFR gene. However, having a common variant in the MTHFR gene does NOT change your medical care.*

What is the MTHFR gene?

MTHFR is a gene that makes an enzyme called **M**ethylene**T**etra**H**ydro**F**olate **R**eductase. This enzyme works with a B-vitamin called folate. Together, MTHFR and folate help to reduce the level of homocysteine (a potentially harmful amino acid). Very high levels of homocysteine may be one risk factor for blood clots and heart disease.

I have an MTHFR variant. What does that mean?

Everyone has two copies of the MTHFR gene, one copy from each parent. If you've been told you have an MTHFR variant, it means you have a difference in either one or both copies of the MTHFR gene. The two most common MTHFR variants are **C677T** and **A1298C**. These variants are very common and not a disease.

DID YOU KNOW?

The exact same genetic variant can go by more than one name.

- **C677T** has also been called c.665C→T or A222V or p.Ala222Val
- **A1298C** has also been called 1298A→C or G429A or p.Glu429Ala

How common are MTHFR variants?

MTHFR variants are found in people worldwide. In the United States, about 1 in 3 people have at least one MTHFR variant and 1 in 10 people have variants in *both* copies of the MTHFR gene.

What happens when an MTHFR variant is present?

The common MTHFR variants cause a minor change in the DNA code. This makes the MTHFR enzyme work a little slower than usual. A person with two copies of the C677T variant might have a slightly higher homocysteine level than someone without C677T. However, that difference does not affect their health. MTHFR variants only have a small impact on your total homocysteine level. Most people with variants have normal levels of homocysteine. There are many other genetic and non-genetic factors that affect homocysteine levels and your risk for blood clots and heart disease.

Are there any medical problems related to MTHFR variants?

The relationship between the common MTHFR variants and many medical problems has been wondered about for decades. Some studies have suggested a possible risk for common medical problems. These include clotting problems, heart disease, stroke, high blood pressure, pregnancy complications, psychiatric disorders, autism, and certain types of cancer. These are all common conditions that affect people with and without MTHFR variants. **Having an MTHFR variant does not predict your risk, diagnose, or help your doctor treat any of these problems.**

The chance for neural tube defects in a fetus may be slightly higher for a pregnant person with 2 copies of the C677T variant. This chance can be lowered by taking folic acid before getting pregnant and during early pregnancy. Experts recommend that **anyone** who is able to get pregnant should take a daily supplement that has 400 to 800 mcg of folic acid. MTHFR testing has no effect on this recommendation.

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Someone in my family has an MTHFR variant. Should I have testing?

There is no need to test your MTHFR status. Variants in the MTHFR gene are very common and finding one (or two) does not change your medical care. In 2013, the American College of Medical Genetics and Genomics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG) advised ***against*** routine MTHFR testing. Since then, more professional medical groups have made the same recommendation.

Does taking extra folate help a person with an MTHFR variant?

Folate is a vitamin our body needs, but there is no known benefit for a person with an MTHFR variant to take more than the recommended daily amount. Everyone should eat a healthy diet with enough folate, regardless of their MTHFR status. It is especially important to get enough folate during pregnancy.

GENETIC TERMS:
Variant – A difference in the DNA code compared to the typical version of a gene.
Heterozygous - When a person has one typical gene and one genetic variant.
Homozygous – When both copies of the gene are the same.
Compound heterozygous – When a person has two different variants.

More about FOLATE and FOLATE SUPPLEMENTS

Folate is also called vitamin B9. It is found in the food you eat. Some foods high in folate include dark green vegetables (spinach, broccoli, asparagus), legumes (lentils, beans, peas), and citrus fruits.

Folate supplements are the synthetic (man-made) forms of folate. The most common folate supplement is folic acid but there are also folic acid derivatives. These are a form of folic acid with slight chemical differences to make them easier for the body to absorb. If you do not get enough folate in the foods you eat, taking folic acid or a folic acid derivative makes sure your body has enough folate. Many breads and cereals have been fortified with folic acid. Prenatal vitamins usually include extra folic acid compared with regular vitamins.

People with common variants in the MTHFR gene do not need a special type of folic acid.
It is safe to take a regular folic acid supplement if needed.

References:
GeneReviews: Methylenetetrahydrofolate Reductase Deficiency (2016)

Hickey et. al., ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. Genetics in Medicine. (2013; reaffirmed 2020)