MTHFR Gene Fact Sheet

What is the *MTHFR* gene and what does it do?

The *MTHFR* gene is one of the many genes found in the human body. Every person has two copies of this gene, and it produces an enzyme that helps build proteins which allow the body to function properly.

The name of the gene is taken from the enzyme that the gene produces. The enzyme is called **m**ethylene**t**etra**h**ydro**f**olate **r**eductase. This enzyme changes folate (also known as vitamin B9) from the form that we ingest through food or vitamins into a new form of folate that our body can use, which allows certain chemicals in the blood (such as homocysteine) to be recycled.

When do genetic variations in *MTHFR* cause disease?

We all have variations in our DNA that make us unique. Some of these variations are **benign** because the gene still functions normally. However, some variants are **pathogenic** because they cause the gene to function incorrectly. Pathogenic variants can lead to disease. Over time, researchers learn more about which variations are benign or pathogenic by finding them in either healthy people or people with certain types of illnesses. Variations in the *MTHFR* gene may make the body less efficient at processing homocysteine. Individuals who have specific variations and a deficiency of folate may experience mildly elevated levels of homocysteine in the blood, called **homocystinuria**.

There are rare pathogenic variants that can cause extremely high levels of homocysteine in the blood and significant childhood illness, but these are typically in other genes and not *MTHFR*. In the rare instances where pathogenic variants in *MTHFR* lead to this illness, the child inherits pathogenic variants from both of their biological parents. If there is a concern for severe homocystinuria based upon symptoms, your child's pediatrician can test levels of homocysteine in the blood.

Early studies suggested that MTHFR variants or mildly elevated homocysteine were thought to be common in individuals with certain health problems including cardiovascular disease, stroke, neural tube defects, recurrent pregnancy loss, and depression. However, we have since learned that these variants are quite common in most people, including people that are healthy. Supplementation of a synthetic form of folate called folic acid has been found to lower homocysteine levels, but this has not significantly improved health outcomes for people with *MTHFR* variations. **Newer studies have shown no link between these *MTHFR* variants and heart disease or recurrent pregnancy loss.**

Because of the new information we have learned,
it is no longer recommended to test for these variants.

What are the common *MTHFR* variants?

- **C677T**: Up to 40% of Caucasian or Hispanic people have one copy of this variant (heterozygous) and have no clinical consequences. Individuals who have two copies of the variant (homozygous) may have higher homocysteine levels and lower folate levels. Up to 15% of Caucasians and 6% of African Americans are homozygous C677T.
- **A1298C:** Up to 20% of most ethnic groups have at least one copy of this variant (heterozygous). There is no clinical risk by having one copy of the A1298C variant. Having two copies (homozygous) is biochemically similar to having one copy of C677T (see above).
- **C677T/A1289C:** Having one copy of C677T and one copy of A1298C (compound heterozygous) may also cause higher homocysteine levels and lower folate levels.

What can I do to stay healthy if I have an *MTHFR* variant?

In 1998, the United States began to fortify grain with folic acid, which has helped to normalize folate levels in the population. There has been no conclusive evidence that additional supplementation with natural forms of folate has any benefit over folic acid. Regardless of whether you have an *MTHFR* variation(s) or not, **the treatment for elevated homocysteine is the same—dietary intervention and supplementation with folic acid and vitamins B6 and B12**. Because folic acid and vitamin B12 toxicities are rare, the risks associated with daily supplementation are low. While **it is recommended for all women of reproductive age to supplement with folic acid with an over-the-counter prenatal vitamin prior to pregnancy**, there is no evidence that this supplementation lowers the risk for cardiovascular disease or other health outcomes.

More Information:
Medline Plus
https://medlineplus.gov/genetics/gene/mthfr/CDC
Center for Disease Control and Prevention
https://www.cdc.gov/ncbddd/folicacid/mthfr-gene-and-folic-acid.html

For further questions, please contact your provider's office.

References

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