

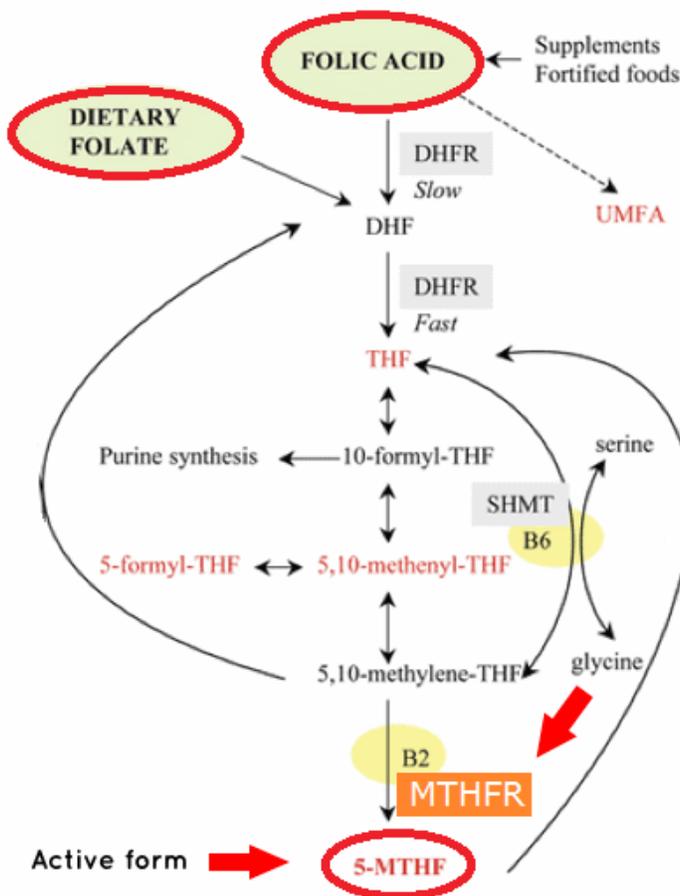
## What is MTHFR, the MTHFR gene, and MTHFR mutation?

MTHFR, short for [Methylenetetrahydrofolate Reductase](#), is a very important *enzyme* in the body.

It's necessary for [Methylation](#) to occur, a metabolic process that switches genes on and off, repairs DNA and many other important things.

Methylation is also essential to convert both folate and [folic acid](#) – each a form of Vitamin B9 – into its *active*, usable form called [5-MTHF](#).

This is a diagram of how complex it is, but you only need to see the final step.



All the steps required to convert folate and folic acid into their active form, 5-MTHF

(Source: Image adapted from [MTHFR Support Aus.](#))

You can see that the final (bottom) step requires MTHFR in order to create the active form.

So without the enzyme activity of MTHFR, methylation of folate and folic acid **cannot occur properly**.

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For a more detailed yet easy to follow explanation of this process, see [Methylation for Dummies](#).

## MTHFR gene

Put simply, the **MTHFR gene** triggers the production of MTHFR enzymes.

Think of the gene as the flower, the enzyme as the honey-bee, and active folic acid as honey.

Without flowers, there will be no honey-bees. Without honey-bees, no honey is created.

## MTHFR mutation



Roughly 30-50% of us carry a mutation in the MTHFR gene, passed down from our parents.

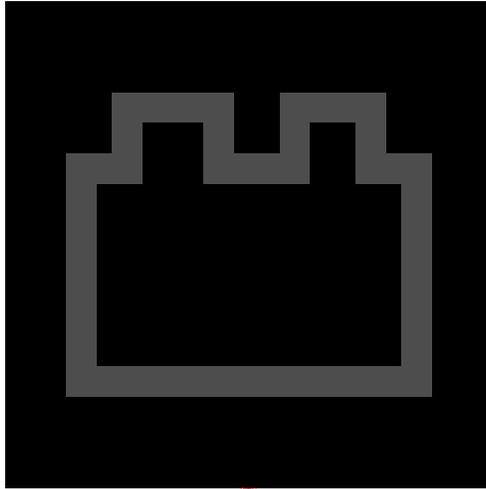
The two main functional mutations (also known as polymorphisms) of the gene are [MTHFR C677T](#) and [MTHFR A1298C](#) (3).

Specifics aside, these genetic mutations are collectively known as **MTHFR mutations**. They can be like a “defect” which limits production of your MTHFR enzymes.

**Most people with a mutation remain unaffected and do not experience symptoms.**

However, for some, enzyme efficiency can drop down to between 30-70% depending on the variant of mutation (4).

Note that there are numerous genetic mutations that can potentially hinder methylation. An MTHFR mutation is just one of many, but it’s the most well-researched and likely most important.



**Summary:** MTHFR is an enzyme necessary for an important metabolic process called methylation. It is this process that converts folate and folic acid into an active form the body can use. The MTHFR gene produces this enzyme, but a genetic mutation can inhibit its function.

## **MTHFR mutation may increase the risk of cardiovascular disease and vitamin B deficiencies**



Those with an MTHFR mutation are at risk for poor MTHFR enzyme efficiency.

Consequently, folate and folic acid cannot be efficiently converted into their active form, known as [5-MTHF](#) or [L-methylfolate](#). Therefore those nutrients can't perform one of their key functions: **breaking down (recycling) Homocysteine**.

[Homocysteine](#) is an amino acid thought to damage the lining of your arteries and other cells of the body. It is naturally formed in the body, but gets broken down (recycled) by 5-MTHF.

Elevated homocysteine levels in the blood is an **independent** risk factor for heart disease, stroke and other forms of cardiovascular disease ([5](#), [6](#), [7](#)).

It has also been linked with a [wide range](#) of other health problems including macular degeneration, Alzheimer's disease, hearing loss, and cancer.

A lack of active folic acid (alongside a low folate diet) can also lead to a [Folate Deficiency](#), which has major health implications on its own.

Therefore, those with a "bad" MTHFR mutation are at an increased risk for health problems if the issue is not addressed and their diet is not rich in folate.

**Summary:** Those with an MTHFR mutation may be predisposed to increased levels of homocysteine, a strong risk factor for cardiovascular disease. They are also more likely to develop a folate deficiency if their diet is not rich in folate.

## What about other disease states and disabilities, like cancer and hypothyroidism?



Considering that genes are influenced by our [diet and environment](#), many studies are also able to find a link between MTHFR and a particular disease process or disability.

This ranges from cancer risk to autoimmune diseases and more; however it's difficult to pinpoint an MTHFR mutation alone as a direct risk factor.

There is a [dubious](#) compilation of the research [here](#), but the studies are far from conclusive and not all the research is listed.

Take thyroid hormone, for example, which appears to help regulate conversion of vitamin B2 ([17](#)). Vitamin B2 is crucial in the methylation of folate (more on that below), so we can make the assumption that those with [hypothyroidism](#) (an under active thyroid) and an MTHFR mutation are high risk. It could be true, yes, but it's still just a theory.

The reality is that overall evidence for these health claims are hypothetical, and MTHFR mutations are unlikely to be a direct causal factor. Innocent until **proven** guilty.

**Summary:** MTHFR could very well contribute to or exacerbate heart disease and folate deficiency, but this is due to excessive homocysteine. The mutation itself is unlikely to be a direct cause of certain disease states or disabilities.

## MTHFR symptoms of a problem



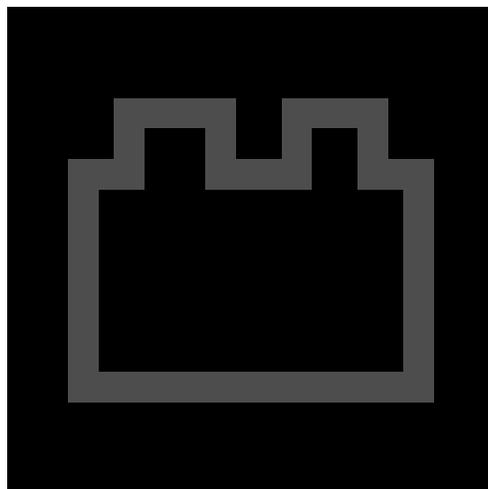
If you believe you may have an MTHFR issue, there is no way to know for sure without getting tested.

In saying that, there are some trending “MTHFR symptoms” among those with a defect that warrant an MTHFR test:

- **High homocysteine levels:** Caused by poor methylation.
- **Folate deficiency:** A deficiency in folic acid (folate) could be linked to MTHFR and is worth checking out. Common symptoms include extreme fatigue, light-headedness, and forgetfulness.
- **Had a miscarriage:** Many [practitioners](#) recommend testing for MTHFR mutations if you have had one or more miscarriages.
- **Longstanding gastrointestinal issues:** Such as [irritable bowel syndrome](#).
- **An autoimmune disease:** Such as [fibromyalgia](#), although this is based more on anecdotes than solid science.
- **Long history of anxiety or depression:** Based more on anecdotes than solid science.

It’s important to note that an MTHFR mutation itself is **not inherently dangerous**... but any form of genetic variance has the possibility to affect your health.

Knowing what the gene is and *how it could affect you* is seen by many as beneficial.



**Summary:** There are some common trends among those who have an MTHFR mutation. If you experience any “MTHFR symptoms” it could be worthwhile getting tested.

## **Folic acid is a problem, 5-MTHF is a solution**



Folic acid is the conventional supplement for treating B-vitamin deficiency, lowering homocysteine levels, and reducing the incidence of [Neural Tube Defects](#) (8, 9).

It is so effective that the addition (fortification) of folic acid to wheat flour is now mandatory in Australia, USA, Canada and several other countries (10).

This is a **big problem** for people who don't metabolise folic acid well, whether from low MTHFR activity or another enzyme issue (11).

It becomes an even bigger problem when you consider the recommended daily intake for folic acid is 400 µg, yet unmetabolised folic acid already appears in the blood when we consume just 200 µg per day (12).

Folic acid accumulating in the blood can potentially *mask* dangerous vitamin B deficiencies such as [megaloblastic anaemia](#).

### **Fortunately there is a somewhat simple solution**

Aside from limiting your intake of fortified wheat flour, folic acid supplements should be replaced with the *active* form: [5-MTHF or L-Methylfolate](#).

It bypasses any MTHFR defects, and is shown to be equally (if not more) effective at increasing plasma folate levels and reducing homocysteine concentrations (13, 14).

5-MTHF is also better absorbed and interacts with fewer medications than folic acid (15).

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So far the *FDA* and *European Food Standards Agency* have approved several products containing 5-MTHF. Many speculate it will soon replace folic acid as the protocol treatment (16).

There are some important factors to consider before taking 5-MTHF though, namely your vitamin B12 levels (and a particular variation of vitamin B12). This is why guidance from a Dietitian or GP that specialises in this area is so important.

That said, I recommend [this L-methylfolate \(5-MTHF\) supplement](#) (disclosure: this is an affiliate link). The reason is because it contains 800 mcg of biologically active folate (5-MTHF) *plus* 1 mg of vitamin B12 (a necessary coenzyme). It is also gluten, dairy and soy-free for those concerned, but always check with your doctor before taking any new supplements.

**Summary:** Folic acid can be very problematic for some, particularly those with an MTHFR mutation. Those people should avoid fortified wheat flour and look to swapping regular folic acid supplements for 5-MTHF.

## Folic acid, MTHFR and pregnancy



Active folic acid is highly protective against Neural Tube Defects.

However, a conventional folic acid supplement is likely not protective of your child if it remains *inactivated* in your blood stream.

That's why testing for and flagging an MTHFR mutation could be especially useful for women of childbearing age.

Therefore, a more conservative and thoughtful approach to folic acid supplementation is warranted for those with MTHFR issues.

If you are planning to have a child, or less than 13 weeks after conception, then **supplement with 5-MTHF instead of folic acid**. The supplement I recommend is listed in the section above, but *always consult with your doctor first*.

While you're at it, you should be avoiding these [6 foods](#) too.

**Summary:** Women with an MTHFR mutation who are planning to have a child or already less than 13 weeks pregnant should be supplementing with 5-MTHF rather than folic acid.

## MTHFR diet and nutrition recommendations



The importance of folate cannot be overstated.

That is why MTHFR symptoms warrant such concern in the first place.

While more folic acid (*synthetic* vitamin B9) is **not** desirable, more folate (*natural* vitamin B9) certainly is.

This is especially true for those with an MTHFR defect, as more folate in the diet means more opportunities to create the [active form 5-MTHF](#). The more lottery tickets you buy, the more opportunities you have to win the lottery.

The body easily recycles leftover folate into a harmless compound, whereas it cannot do so with folic acid. Without getting into chemistry, that is why folate does not accumulate in the blood, but folic acid does.

According to [NutritionData](#), the best sources of folate per 100 g serving are:

- Beans and lentils (~50% RDI)
- Raw spinach (49% RDI)
- Asparagus (37% RDI)
- Romaine (Cos) lettuce (34% RDI)
- Broccoli (27% RDI)
- Avocado (20% RDI)
- Oranges/Mangoes (~10% RDI)

(RDI = *Recommended Daily Intake*)

Studies have even shown that a folate-rich diet can match the homocysteine-lowering effects of either a regular folic acid or 5-MTHF supplement ([16](#)).

As though we needed any additional reasons to eat more vegetables and legumes.

There are several other important nutrients to think about for folate metabolism. Namely [vitamin B2](#) (Riboflavin) and [vitamin B6](#) (Pyridoxine), which assist in the formation of 5-MTHF.

The best sources of vitamin B2 per 100 gram serving are:

- Almonds (60% RDA)

- Beef and lamb (51% RDA)
- Oily fish (34% RDA)
- Hard boiled eggs (30% RDA)
- Mushrooms (29% RDA)
- Spinach (14% RDA)
- Natural yoghurt (~14% RDA)

The best sources of vitamin B6 per 100 gram serving are:

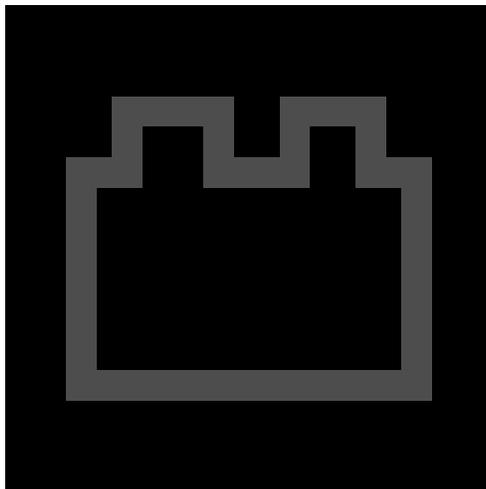
- Sunflower seeds (67% RDA)
- Pistachio nuts (56% RDA)
- Oily fish (40-50% RDA)
- Turkey, chicken, pork and beef (34-40% RDA)
- Bananas (18% RDA)
- Avocados (14% RDA)
- Spinach (~12% RDA)

If you are deficient in either of these nutrients, part of the folate metabolism cycle will break down.

### What foods to avoid?

It is commonly thought that antacids, some [blood pressure](#) medications, metformin (for [type 2 diabetes](#)), and contraceptives may all inhibit dietary absorption of B-vitamins to some extent.

If you regularly take any of these, it is best to seek personalised health advice from your Dietitian or doctor.



**Summary:** Natural folate is a nutrient that we all need to eat more of... MTHFR defect or not. Vitamins B2 and B6 are also important given their role in folate metabolism.

## How and where to get an MTHFR test



Only a genetic test can verify if you have a gene mutation, and what specific type.

Most service providers can mail the testing kit out to you, so it remains non-invasive and you don't have to go anywhere. Simply send back a saliva swab and await your results.

The biggest and most well-known company that caters worldwide is *23andme*. They have over 1 million customers, and provide the most comprehensive genetic profile as it relates to methylation and the MTHFR gene.

You can see more details and order your own kit at [23andme.com](https://www.23andme.com).

Additionally, instead of trying to interpret your own results, you can run your *23andme* methylation analysis through [GeneticGenie.org](https://www.GeneticGenie.org) (free) and it helps to explain the basics of what you need to know.

If instead you choose to use your own local lab, ensure they test for the [MTHFR C677T and A1298C mutations](#), which are the main ones. Not all labs do so make sure you ask first.

**Remember that genetic testing is only a tool to support you in better health.** Having a genetic mutation *does not* necessarily mean it will affect you.

As they say, “*Genes load the gun, environment pulls the trigger.*”

Always consult with a Dietitian or GP who can put your results into context. And eat more folate-rich foods... That goes for everybody.