

LEVEL 1 · FUNDAMENTALS · METHYLATION

The Folate Cycle Explained

Folate is not a methyl group. It is the vehicle that carries one — and understanding it as a delivery system rather than an ingredient makes the whole MTHFR conversation make sense.

By **Shaaf Hussain** · Author & Founder | Level 1 · Fundamentals | Educational — not medical advice

<https://longevitydecoded.net/the-folate-cycle-article.html>

WHAT YOU'LL UNDERSTAND BY THE END

What folate actually does, why it is drawn as a loop, where the branch point sits, and why one enzyme in that loop became famous.

Folate has a reputation problem in both directions. It is either treated as a pregnancy nutrient and otherwise ignored, or as the center of an elaborate supplement protocol. Neither describes what it does.

Folate is a carrier. Its job is to pick up a one-carbon unit at one place in the cell and put it down at another. It is not consumed in the process — it goes back for more.

THE RIGHT MENTAL MODEL

A vehicle, not a cargo

The distinction matters because it explains a persistent confusion. People ask whether they are getting enough methyl groups and reach for folate, as though folate *were* the methyl group. It is not. The carbon comes from amino acids, as the last lesson covered. Folate is the vehicle that moves it.

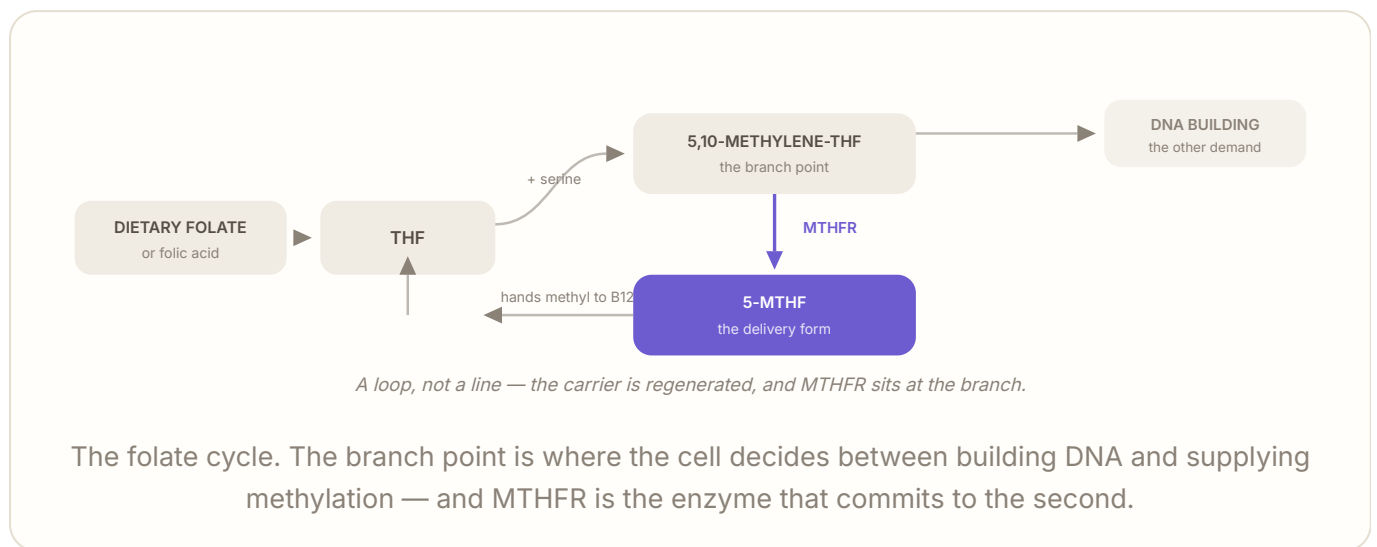
So a folate shortage does not mean the raw material has run out. It means the delivery fleet is too small, or too much of it is parked in a form that cannot be reloaded. Those are different problems with different causes, and they need

different answers.

HOW IT RUNS

The loop, and the fork in it

Folate enters as either dietary folate or folic acid and is converted into **THF**, the working form. Serine loads a one-carbon unit onto it, producing **5,10-methylene-THF** — and here the cycle reaches a fork.



- **One way builds DNA.** The unit is handed to nucleotide synthesis, for a cell that is about to divide.
- **The other way supplies methylation.** An enzyme called **MTHFR** converts the carrier into **5-MTHF**, the delivery form.

5-MTHF then hands its methyl group to vitamin B12, which passes it into the methionine cycle — the loop from the first lesson. Having delivered, the carrier returns to THF and the circuit starts again.

WHY MTHFR BECAME THE FAMOUS ONE

MTHFR sits exactly at the fork, and the step it catalyzes is effectively **one-way**. Once the cell has committed a unit to methylation, it does not easily send it back to DNA building. An enzyme at a committed branch point is a natural control valve, which is why it attracted attention — and, unfortunately, why a common variation in it became an internet diagnosis. What the variants actually do, and do not do, is a Level 4 lesson.

THREE WORDS, THREE THINGS

Folate, folic acid and 5-MTHF

These get used interchangeably and are not the same:

- **Folate** — the general term, and the form in food. Leafy greens, legumes, liver.
- **Folic acid** — a stable synthetic form used in supplements and in food fortification. It requires conversion before the body can use it.
- **5-MTHF** — the already-converted delivery form, sold as “methylfolate”.

It is often claimed that the converted form is universally superior. That overstates what the evidence supports. Fortification with folic acid produced one of the clearest public-health wins of the last few decades — a substantial fall in neural tube defects — so a form that “does not work” plainly does work. Whether the converted form is better *for particular people* is a narrower and much less settled question, and it belongs with a clinician rather than a search engine.

THE HANDOFF

Where B12 comes into it

The handoff from 5-MTHF into the methionine cycle needs vitamin B12. Without enough of it, that step stalls — and folate accumulates in the 5-MTHF form, unable to hand off its cargo and unable to return to THF for other work.

The fleet is not missing. It is stuck, loaded, in the wrong place. That is a real and well-described phenomenon, and it is the clearest illustration of why this system has to be understood as a loop: a blockage at one point starves everything downstream of it while backing up everything behind.

WHAT THE EVIDENCE ACTUALLY SAYS	
HUMAN EVIDENCE	The structure of the folate cycle, and B12's role in the handoff to methionine, are established biochemistry.
HUMAN EVIDENCE	Folic acid fortification substantially reduced neural tube defects at population level — one of the best-documented nutritional public-health interventions there is.
MECHANISM	That folate can become trapped in the 5-MTHF form when B12 is inadequate is well described mechanistically and clinically relevant in deficiency.
UNCERTAIN	Whether 5-MTHF supplements outperform folic acid in people without deficiency or malabsorption. Studied, genuinely unsettled.
NOT SUPPORTED	That folic acid is harmful or useless, or that everyone should take the methylated form.

CONNECTED SYSTEMS

Where this connects

MITOCHONDRIAL & CELLULAR ENERGY Methylation: The Hidden Supply Chain	METABOLIC & INSULIN SENSITIVITY The Metabolic Triangle: Gut, Methylation & Mitochondria
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THE WHOLE LESSON IN ONE LINE

Folate is the vehicle that carries one-carbon units, not the cargo itself — it runs as a loop with a one-way fork between building DNA and supplying methylation, and MTHFR is simply the enzyme standing at that fork.

Educational content only — not medical advice, diagnosis, or treatment. This lesson explains general biochemistry for a non-specialist audience. It does not diagnose any condition and does not recommend any supplement, dose or protocol for any individual. Methylation cannot be assessed from symptoms, and no article can tell you whether yours is working well. Genetic variants, homocysteine and B-vitamin status should be interpreted by a qualified clinician in the context of your full history. Discuss any changes to your health, medications, or supplements with a licensed professional who knows your situation.

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