LEVEL 1 · FUNDAMENTALS · METHYLATION

One-Carbon Metabolism: The Engine Behind Methylation

Methylation spends methyl groups. Something has to supply them — and that supply line is shared with the job of building new DNA, which is why it behaves like a budget rather than a tap.

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

https://longevitydecoded.net/one-carbon-metabolism-article.html

WHAT YOU'LL UNDERSTAND BY THE END

Where one-carbon units come from, why the same pool serves two very different jobs, and why “more methyl donors” is the wrong mental model.

The previous lesson ended on a loop: nutrients supply methyl groups, SAM donates them, and what is left gets recycled. This lesson is about the supply end of that loop — the part that decides how much there is to spend.

The umbrella term is **one-carbon metabolism**. It is a slightly awkward name for a simple idea: a set of reactions that move single carbon atoms around, ready to be attached to whatever needs them.

THE SOURCES

Where the units come from

One-carbon units are not eaten directly. They are stripped from ordinary molecules you already have, mostly amino acids:

- **Serine** — the largest single contributor in most tissues. It hands a carbon to the folate pool and becomes glycine in the process.
- **Glycine** — can be broken down to release a one-carbon unit of its own.

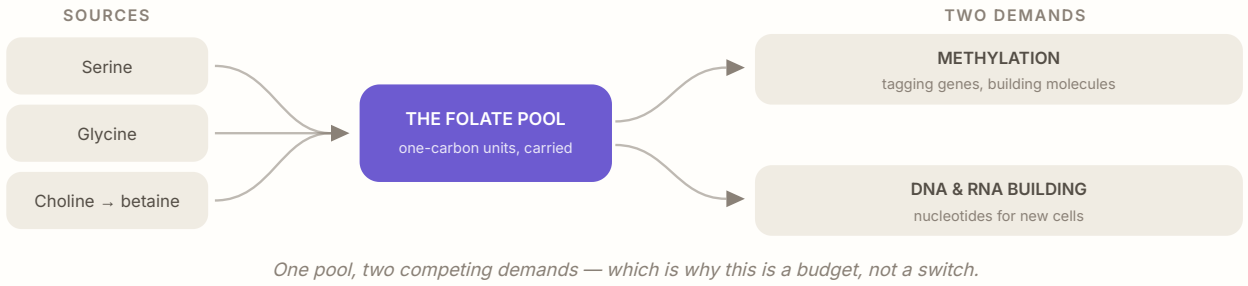
- **Choline** — converted to betaine, which can donate a methyl group directly, bypassing folate entirely. This alternative route matters most in the liver.
- **Histidine and formate** — smaller contributors, but real.

Note what is *not* on that list: a supplement. The main inputs are protein-derived amino acids and a nutrient found in eggs, liver and soy. Folate and B12 do not supply the carbon — they **carry and transfer** it, which is a different job and a common source of confusion.

WHY IT IS A BUDGET

One pool, two demands

Here is the part that reframes everything. The folate pool does not only feed methylation. It also supplies the raw material for building **new DNA and RNA** — the nucleotides a cell needs in order to divide.



One pool, two competing demands — which is why this is a budget, not a switch.

The same one-carbon pool feeds two jobs: tagging molecules, and building the nucleotides for new cells.

Those two jobs draw on the same supply. A tissue turning over rapidly — bone marrow, gut lining, a healing wound — is spending heavily on the building side. That is a real demand, not a metaphor, and it is why folate requirements rise in states of rapid cell division.

THE SINGLE MOST USEFUL IDEA IN THIS SCHOOL

Methyl supply is a **budget**, not a tap. It has competing claims on it, it varies by tissue and by circumstance, and the body prioritizes. This is why "take more methyl donors" is the wrong shape of answer to almost every question about methylation — it assumes a tap that is running dry, when the actual system is an allocation problem that is mostly working.

WHERE IT GOES

The biggest single spender

On the methylation side, one job dominates. **Creatine synthesis** is among the largest consumers of methyl groups in the body — a surprisingly large share of the total, spent on one molecule that muscle and brain use as an energy buffer.

This is a genuinely interesting piece of biochemistry, and it is worth flagging early because it explains something counterintuitive: a substantial part of your methylation capacity is committed before any question of gene regulation arises. The system is not idling, waiting to be optimized. It is already busy.

THE SHAPE OF IT

Why the cycles are drawn as circles

Both the folate cycle and the methionine cycle are usually drawn as loops, and that is not decoration. Carriers are *regenerated* rather than consumed: a folate molecule picks up a one-carbon unit, hands it off, and returns to pick up another.

The practical consequence is that a shortage can appear in two quite different ways — too few carriers, or carriers stuck in a form that cannot be reused. Those look similar from the outside and have different causes. Level 2 takes that apart properly.

WHAT THE EVIDENCE ACTUALLY SAYS

HUMAN EVIDENCE	One-carbon metabolism supplying both methylation and nucleotide synthesis is established biochemistry, demonstrated across decades of work.
HUMAN EVIDENCE	Folate requirements rise during rapid cell division — pregnancy being the best-studied case, where adequate folate reduces neural tube defects. This is guideline-level evidence.
MECHANISM	That creatine synthesis represents a large share of methyl-group demand is well characterized biochemically; what it means for anyone's day-to-day methylation is much less clear.
UNCERTAIN	Whether supplemental creatine meaningfully spares methyl groups for other uses in healthy people. Biologically plausible, studied, not settled.
NOT SUPPORTED	That increasing methyl-donor intake beyond sufficiency improves health outcomes in people who are not deficient.

CONNECTED SYSTEMS

Where this connects

MITOCHONDRIAL & CELLULAR ENERGY

Methylation: The Hidden Supply Chain

NUTRITION & GUT HEALTH

The Gut: The Root System

THE WHOLE LESSON IN ONE LINE

One-carbon metabolism supplies the units methylation spends — from amino acids rather than supplements — and because the same pool also builds DNA, methyl capacity behaves like a budget with competing claims, not a tap that can simply be opened wider.

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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